I. CASTOR OIL METAMORPHOSIS : THE RE-STRUCTURING OF CASTOR OIL SYNTHONS TO INSECT SEX-PHEROMONES

II. STUDY OF THE THERMAL TRANSFORMATION OF CASTOR OIL

By

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DEPARTMENT OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY KANPUR

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A Thesis Submitted
in Partial Fulfilment of the Requirements
for the Degree of

DOCTOR OF PHILOSOPHY

By

RAAJ KUMAR

to the

DEPARTMENT OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY KANPUR

AUGUST, 1981

IN

FOND MEMORY OF

MY MOTHER

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology Kanpur, India, under the supervision of Professor S. Ranganath

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

Raaj Kumar

CERTIFICATE

Certified that the work contained in this thesis, entitled,

I. CASTOR OIL METAMORPHOSIS: THE RE-STRUCTURING OF CASTOR OIL SYNTHONS TO INSECT SEX-PHEROMONES.

II. STUDY OF THE THERMAL TRANSFORMATION OF CASTOR OIL

has been carried out by Mr. Raaj Kumar under my supervision and the same has not been submitted elsewhere for a degree.

S. Ranganathan
Thesis Supervisor

Kanpur
August 1981.

DEPARTMENT OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY, KANPUR, INDIA

CERTIFICATE OF COURSE WORK

This is to certify that Mr. Raaj Kumar has satisfactorily completed all the course requirements for the Ph.D. degree programme. The courses include:

Chm	501	Advanced Organic Chemistry I
Chm	502	Advanced Organic Chemistry II
Chm	521	Chemical Binding
Chm	523	Chemical Thermodynamics
Chm	541	Advanced Inorganic Chemistry I
Chm	581	Biochemistry
Chm	618	Frontier Topics in Organic Chemistry
Chm	620	Frontier Topics in Biochemistry
Chm	600	Biosynthesis of Natural Products
Chm	500	Mathematics for Chemists
Chm	800	General Seminar
Chm	801	Graduate Seminar
Chm	900	Graduate Research

Mr. Raaj Kumar successfully completed his Ph.D. qualifying examinations in January 1977.

(U.C. Agarwala)
Professor and Head
Department of Chemistry

(P.C. Nigam)
Convener
Departmental Post-graduate Committee

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RAAJ KUMAR

PREFACE

The thesis entitled, "I. Castor oil metamorphosis: The transformation of castor oil synthons to insect sex pheromones II. Study of the thermal transformation of castor oil" endeavours to illustrate the versatility of this unusual, yet abundant, molecule as a veritable fountain for useful synthons and for the understanding of novel facets of reaction mechanisms.

The key synthons, methyl 11-oxo (E) 9-undecenoate, methyl 10-oxo (E) 8-decenoate, 1-tetrahydropyranyloxy 11-undecyne and 1-tetrahydropyranyloxy 10-decyne, have been prepared, in good overall yields, from castor oil. These, in turn, have been effectively used in the syntheses of, in good yields and high stereochemical purity, the insect sex pheromones, a. 1-acetoxy (E) 9,11-dodecadiene, b. (E,E) 8,10-dodecadien 1-ol, c. (Z) 10-tetradecen 1-ol, d. 1-acetoxy (Z) 9-tetradecene, e. 1-oxo (Z) 9-tetradecene, f. ethyl (Z) 9-tetradecenoate, g. 1-acetoxy (Z) 9-dodecene, h. 1-acetoxy (Z,E) 9,11-tetradecadiene, related to the species a. Diparopsis castanea (red bollworm moth, cotton pest), b. Laspeyresia pomonella (codling moth, apple orchard pest), c. Archips semiferanus (oak leaf roller), d. Spodoptera frugiperda (fall armyworm moth, apple orchard pest), e. Heliothis virescens (tobacco budworm, tobacco pest), f. Bombus lucorum (bumblebee), g. Paralobesia viteana (grape berry moth, vineyard pest) and h. Prodenia eridania (southern armyworm moth).

The thermal fragmentation of castor oil has been demonstrated to proceed *via* a clean $\pi^2s + \sigma^2s + \sigma^2s$ pathway. Thus, methyl 12-hydroxy 9-octadecynoate, prepared from castor oil *via* sequence, Br_2 addition, alkali mediated elimination and esterification gave, on thermolysis, cleanly, the allene, methyl 9,10-undecadienoate and heptanal. This fragmentation also constitutes the first example of a $\pi^2s + \sigma^2s + \sigma^2s$ process with γ , δ -unsaturated acetylenic alcohols. The transition state in the $\pi^2s + \sigma^2s + \sigma^2s$ fragmentation of γ,δ -unsaturated alcohols highlights the importance of the $\alpha - \beta$, C-C scission. This has been demonstrated by a study of several α -substituted γ,δ -unsaturated alcohols. A novel and practical procedure for the PhCHO $\longrightarrow$ PhCDO change has been developed involving the $\pi^2s + \sigma^2s + \sigma^2s$ fragmentation of γ,δ -unsaturated alcohols. An integrated mechanistic rationalization has been presented for the complicated events that take place on thermolysis of castor oil in presence of alkali. The overall process involves a primary, invariable, set of events which is followed by a milieu of transformations proceeding *via* coupled and uncoupled events. The secondary changes can be directed by internal or external controls. The understanding of this change has led to the identification of "castor soap" as an efficient agent for a. the reduction of non-enolizable ketones, b. Wolff-Kischner reduction, c. the generation of carbenic intermediates and d. for a practical $ArNO_2 \longrightarrow ArNH_2$ change.

CONTENTS

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CHAPTER I

CASTOR OIL METAMORPHOSIS: THE RE-STRUCTURING OF CASTOR OIL SYNTHONS TO INSECT SEX-PHEROMONES

I.A. INTRODUCTION

The advent of pesticides was rightfully hailed in an era where the technology of agricultural production was at a primitive stage and the principal concern was the protection of crops from harmful insects. Indeed the dogma that chemical insecticides are saviours of mankind was so firmly entrenched that when Rachael Carson voiced her apprehension of the wide use of insecticides in a series of brilliant articles in "New Yorker", few agreed with her ! That was in 1962. In retrospect, the book "Silent Spring", has made mankind aware of the need for symbiosis with Nature and has led to numerous measures for the protection of environments on the one hand, and for the selective destruction of harmful agents on the other. Insect sex pheromones belong to this category. These highly active, generally non-toxic and insect specific attractants have been demonstrated as capable of pest control. Thus, they can be effectively used in

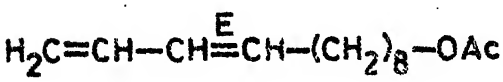
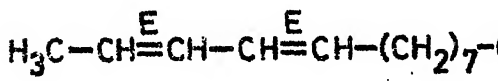
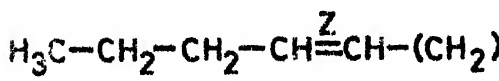
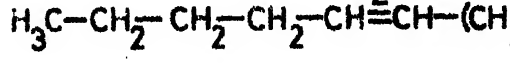
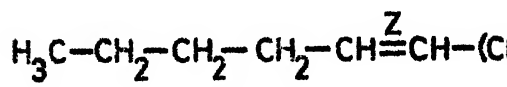
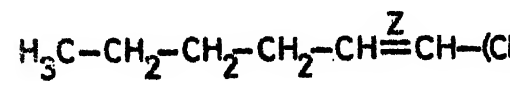
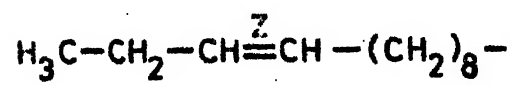
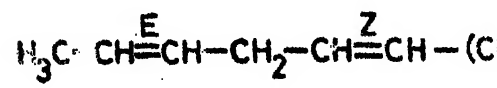
sampling and monitoring specific pest populations, in attracting insects to traps or poison baits kept away from standing or harvested crops,and in distracting insects from their normal mating behaviour. Although no pheromone has been fully registered for use in crop protection, survey and monitoring traps incorporating synthetic sex pheromones have been widely used for measuring the presence and abundance of pest populations and are commercially available.

In a tropical country like ours insect sex attractants can play a pivotal role,particularly with reference to the protection of cereal crops, tea, cotton and tobacco. Sex pheromones are so thinly spread amongst vast insect populations that their isolation from natural sources is not at all a practical proposition. Consequently synthetic routes to these are important. In the past decade there has been a tremendous interest in the synthesis of insect sex pheromones. From a synthetic vantage point, they exhibit deceptively simple structures. In reality however, their synthesis pose, endowed as they are generally with - on a linear saturated carbon chain - terminal functional groups and stereochemically specific π , multiple π and skipped π systems, formidable strategic and experimental challenges and our present endeavours in this area have amply attested to these !

In the present work,Indian castor oil has been transformed to pheromones presented in CHART I.A.1. It was considered

CHART 1.A.1

Insect sex pheromones prepared in the present work (I.C) from Indian castor oil

Pheromone	Related species
	Diparopsis castanea (Red bollworm)
	Laspeyresia pomonella (Codling moth)
	Archips semiferanus
	Spodoptera frugiperda
	Bombus lucorum
	Heliothis virescens
	Paralobesia viteana
	Prodenia eridania

appropriate to provide a background that has as the focus the synthetic routes thus far available to these. Such an account is presented in Section I.B.(Background).

I.B. BACKGROUND

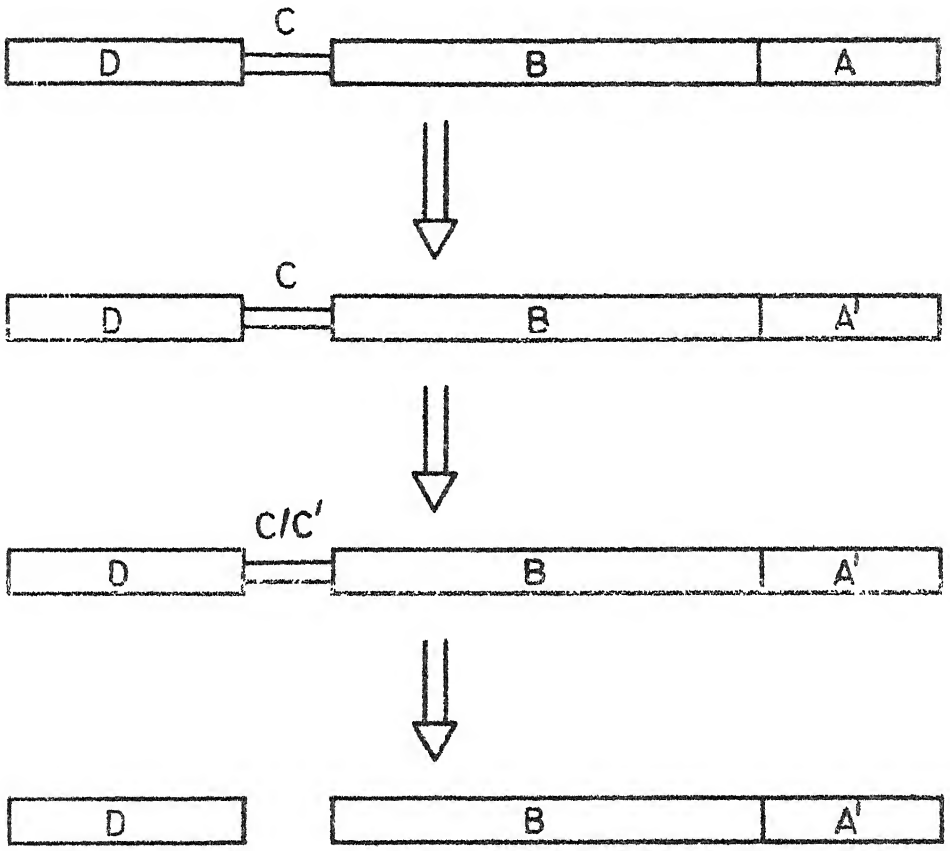
The great majority of the synthetic routes to insect sex pheromones can be antithetically analysed in terms of, the preparation of, separately, the hydrophilic head fragment, the hydrophobic tail fragment, their union either involving a σ bond or with synchronous or subsequent creation of the specific π system and the further trivial functional group modification (CHART I.B.1). The task then is the choice of the two fragments and the methodology for the introduction of the uniting C-C bond. Surprisingly, whilst the individual units are prepared by a variety of procedures, their union is brought about by a handful of popular methods. Consequently, the background material is presented with emphasis on the reaction that unites the fragments and the synthesis of individual fragments are given wherever there are appealing facets. The synthetic routes which cannot be so easily classified are described at the end of this section.

Synthesis of insect sex pheromones by Wittig reaction

The versatility of the Wittig reaction, in terms of the diverse phosphonium salts that could be accomodated and in terms of reaction conditions that can largely give rise to either the E or Z π system, has made it a popular choice in pheromone

CHART 1.B.1

Strategy generally used in insect sex-pheromone syntheses



A = Functional group A' = Masked functional group.

BA = Hydrophilic head fragment.

C = π or σ bond. C' = modified π bond.

D = Hydrophobic tail fragment.

synthesis. This facet is illustrated in CHART I.B.2 and CHART I.B.3.

Synthesis of pheromones of the type, $H-(CH_2)_m-\overset{Z}{CH=CH}-(CH_2)_{n-1}-OAc$

Insect sex pheromones,possessing a single π system of Z stereochemistry, such as, Spodoptera frugiperda, Bombus lucorum, Heliothis virescens and a host of related compounds have been synthesised using the Wittig reaction. Stereochemical purity in the range 80-95% can be achieved by an appropriate choice of the base used in the preparation of the phosphorane, the solvent and with rigorous control on the reaction time and temperature. A detailed study of the stereochemical controls in the Wittig reaction as a function of reaction conditions, that is of particular relevance relating to the synthesis of insect sex pheromones, has been carried out with ethyl 8-oxo oct(Z) 4-enoate and triphenyl n-pentyl phosphonium bromide, giving rise to both Z,Z and Z,E isomers of ethyl trideca 4,8-dienoate.[1] The details of this important investigation are presented in CHART I.B.4. In general, conditions that favour a syn-erythro transition state favour the formation of Z olefins. This can be accomplished by effecting a kinetic control and by preventing the initially formed adduct to equilibrate to the thermodynamically favoured threo principally by complexation with lithium ions.[2]

CHART 1.B.2

Synthesis of pheromones of the type, $H-(CH_2)_m-CH\overset{Z}{=}CH-(CH_2)_{n-1}-OAc$ by Wittig reaction.

Ref	Aldehyde	Phosphonium salt	Reaction conditions
3	$H-(CH_2)_m-CHO$ m = 2, 3.....	$Ph_3\overset{+}{P}-CH_2-(CH_2)_{n-1}-OH\ Br^-$ n = 8, 9, 10, 11	Not given
4, 5	$H-(CH_2)_m-CHO$ m = 2 → 7	$Ph_3\overset{+}{P}-CH_2-(CH_2)_{n-2}-COOH\ Cl^-/Br^-$ n = 6 → 9	NaH, DMSO
6	$AcO-(CH_2)_8-CHO$	$Ph_3\overset{+}{P}-CH_2-(CH_2)_3-CH_3\ X^-$	$NaN[Si(CH_3)_3]_2$ THF, −78°
7	$AcO-(CH_2)_m-CHO$ m = 8, 10	$Ph_3\overset{+}{P}-CH_2-(CH_2)_{n-1}-H\ Br^-$ n = 1, 2, 3, 4	K, HMPT
7	$HOOC-(CH_2)_8-CHO$	$Ph_3\overset{+}{P}-CH_2-(CH_2)_{n-1}-H\ Br^-$ n = 1, 2, 3, 4	K, HMPT
8	$MeO-(CH_2)_8-CHO$	$Ph_3\overset{+}{P}-CH_2-(CH_2)_{n-1}-H\ X^-$ n = 0 → 5	K, HMPT

CHART 1.B.3

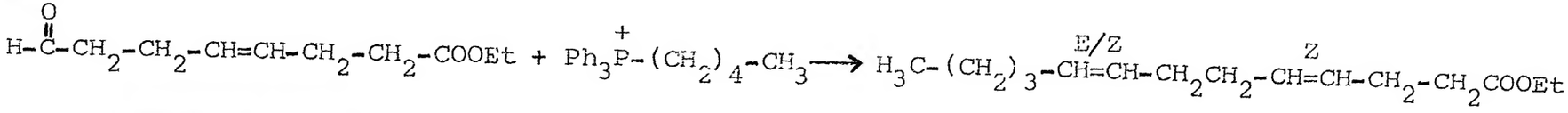
Synthesis of pheromones of the type,

$H-(CH_2)_m-CH\overset{E}{=}CH-CH\overset{E}{=}CH-(CH_2)_{n-3}-OAc$ by Wittig reaction

Ref.	Aldehyde	Phosphonium salt	Reaction conditions
9	$AcO(CH_2)_8CHO$	1. $Ph_3\overset{+}{P}CH_2-CHO\ X^-$ 2. $Ph_3\overset{+}{P}-CH_3\ X^-$	$NaN[Si(CH_3)_3]_2$ THF, -78°
10	$AcO(CH_2)_8CHO$	$Ph_3\overset{+}{P}-CH_2-CH=CH_2\ Br^-$	n-BuLi, ether
11	$HO-(CH_2)_8-CH\overset{E}{=}CH-CHO$	$Ph_3\overset{+}{P}-CH_3\ X^-$	NaH, DMSO
12	$THPO-(CH_2)_8-CH\overset{E}{=}CH-CHO$	$Ph_3\overset{+}{P}-CH_3\ X^-$	NaH, DMSO
13,14,15	$MeOOC-(CH_2)_6-CHO$	$Ph_3\overset{+}{P}-CH_2-CH\overset{E}{=}CH-CH_3\ Br^-$	NaOMe, DMF, 2hr
16,17	$CH_3-CH\overset{E}{=}CH-CHO$	$Ph_3\overset{+}{P}-(CH_2)_7COOR\ Br^-$ (R = H, Me)	Not given
18	$THPO-(CH_2)_7-CHO$	$(EtO)_2\overset{O}{\overset{\|\|}{P}}-CH_2-CH\overset{E}{=}CH-COOEt$	NaH, diglyme

Chart I.B.4

A study of the stereochemical control in the Wittig reaction,



Ylid formation				Olefin formation			Isomer ratio(%)		Yield(%)
Base	Solvent	temp(°C)	time(hr)	Solvent	temp(°C)	time(hr)	Z	: E	
tBuOK	THF	25	0.5	THF	25	0.8	94	6	69
NaH	DMF	25	2.0	DMF	25	2.0	94	6	59
n-BuLi	Ether	25	1.0	DMF	25	2.0	94	6	68
$NaNH_2$	liq NH_3	-33	1.75	benzene:hexane (1:1)	0°	2.0	94	6	52
NaOEt	DMF	25	1.0	DMF	25 60	2.0 96	92	8	10
n-BuLi	Benzene	25	1.0	Benzene	25	2.0	87	13	49
n-BuLi	THF	-20	1.0	THF	25	1.0	86	14	57
n-BuLi	Ether +1 eq. t-BuOH	25	1.5	Ether +1 eq. t-BuOH	25	1.0	82	18	45
n-BuLi	Ether	25	1.5	Ether	25	2.0	78	22	61

contd..

...contd.

n-BuLi	Ether	25	0.5	Ether +1.1 eq. $LiN(CHMe_2)_2$	-78 -78 to -50	0.5 1.5	78	22	36
n-BuLi	Ether	25	0.5	Ether +t-BuOH	-50 -50 25	1.25 4.5 12.0	78	22	67
n-BuLi	Ether	25	0.5	Ether $+(Et)_3COH$	-40 -40 25	1.3 3.3 12	75	25	67
n-BuLi	Ether	25	0.5	Ether $+CH_3CH(OH)CH_3$	-40 -40 25	1.0 3.0 1.0	71	29	53
n-BuLi	Ether	25	0.5	Ether +EtOH	-40 -40 25	1.3 0.2 1.0	49	51	63
n-BuLi	Ether	0	0.5	Ether +EtOH	-78 -78 to -50 25	1.0 4.5 12	31	69	54
n-BuLi	Ether	0	0.5	Ether +MeOH	-40 -40	1.5 4	25	75	35

Although there is rarely any uncertainity about the occurrence of the Wittig reaction, the process is capricious in the sense that the yield and isomer ratio is highly sensitive to variation of each of the factors involved in the reaction. Nevertheless this reaction has enjoyed wide application. CHART I.B.2, relating to pheromones possessing single π bonds, illustrates how wide variations in substrates can be accomodated. Thus, the phosphonium salts could accomodate a wide range of functional groups such as -OH, -COOH, -OAc etc. Whilst in most cases the genesis of the carbonyl as well as the ylid component is *via* anticipated procedures, there are few exceptions which have noteworthy features. The synthesis of 9-acetoxy nonan 1-al has been achieved by reduction of a thio-ester. The nascent aldehyde was protected by N,N'-diphenyl ethylene diamine (CHART I.B.5)[6].

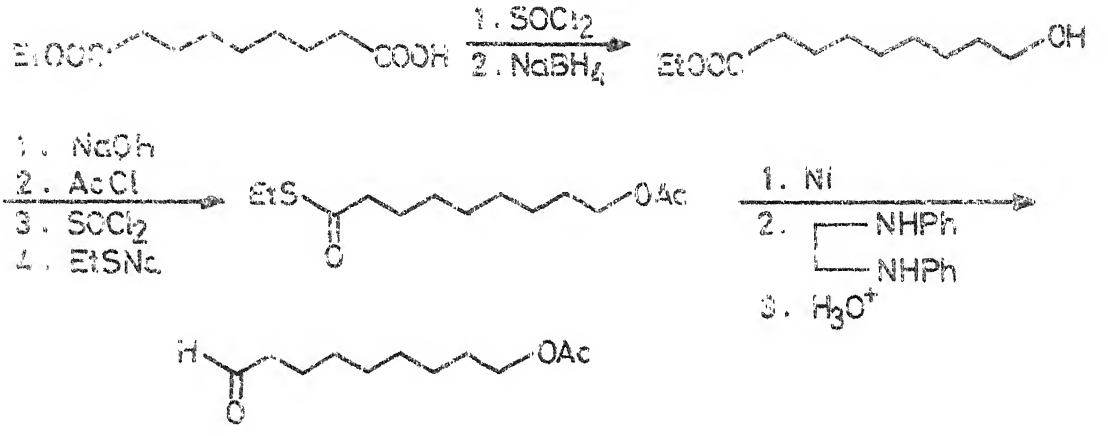
Synthesis of pheromones of the type,

$$H-(CH_2)_m-CH\overset{E}{=}CH-CH\overset{E}{=}CH-(CH_2)_{n-3}-OAc$$

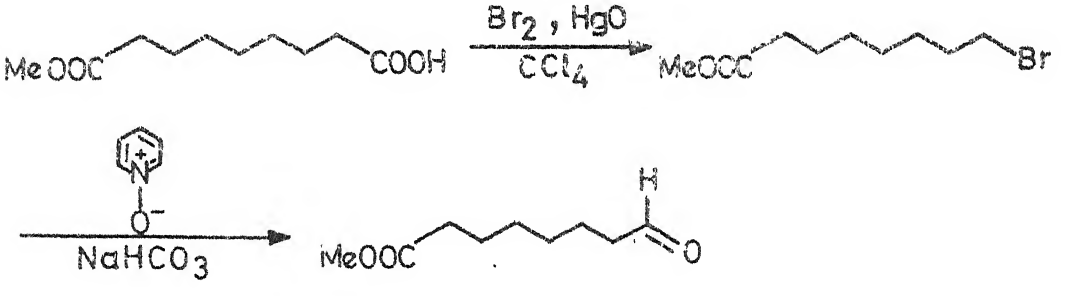
Pheromones having potential for protection of important agricultural crops from pests such as bollworm moth and codling moth belong to this category and consequently their syntheses have attracted interest. In CHART I.B.3 are presented synthetic routes of relevance to the present work. The 1,3-diene unit has been generated with a wide variation in the nature of the two components, either sequentially *via* double Wittig reaction or

CHART 1.B.5

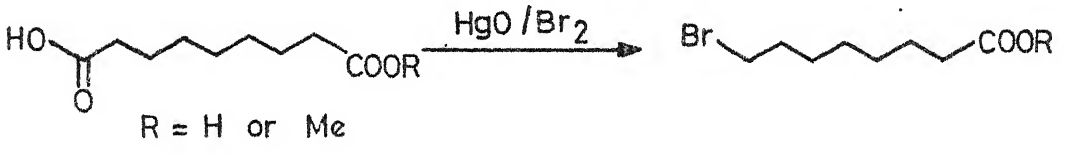
a. Synthesis of 9-Acetoxy nonan-1-al



b. Synthesis of 8-Carbomethoxy octan-1-al



C. Synthesis of 8-bromo 1-octanoic acid



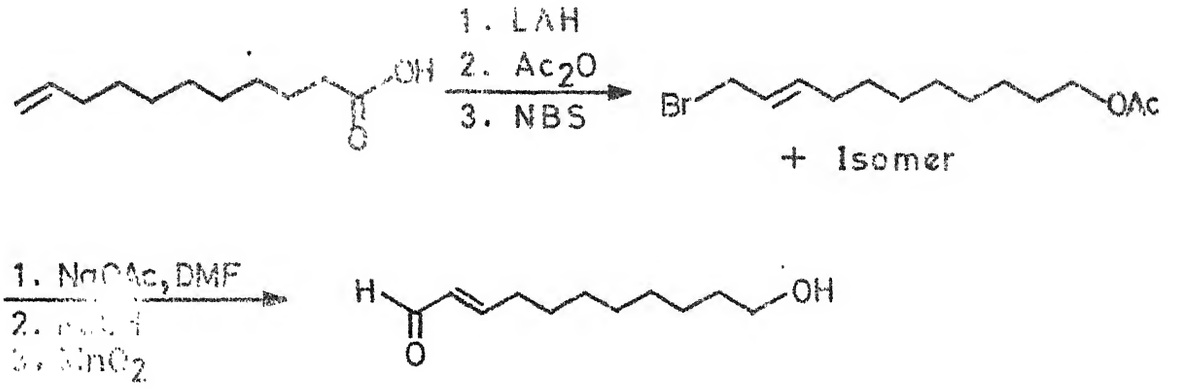
R = H or Me

with substrates already possessing single π bond. The stereochemistry of this unit does not pose a problem since the isomers can be readily equilibrated to the E,E by treatment of hexane solutions with catalytic amounts of iodine under thermal or solar irradiation.[13-15,17] The bollworm moth pheromone possessing the terminal methylene unit has been prepared by methylenation of suitable α , β -unsaturated aldehydes. Such systems having a methylene chain interposed between the α , β -unsaturated aldehyde unit and an appropriate head group, have become important synthons relating to the preparation of a host of natural products. (Please see present work I.C.). Consequently, synthetic routes to them are noteworthy and two procedures related to CHART I.B.3 are presented in CHART I.B.6.[11,12]

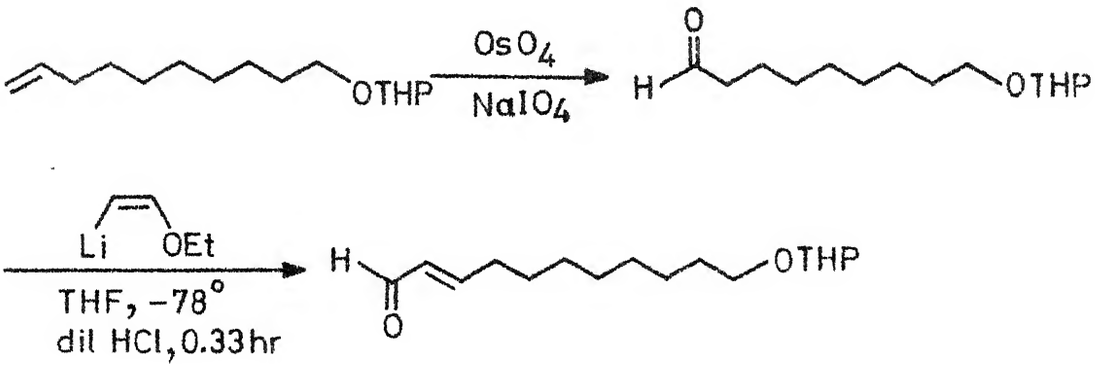
CHART I.B.6.a illustrates the synthesis of the requisite unit <u>via</u> non-stereospecific allylic bromination of 1-acetoxy undec 10-ene, separation of the 11-bromo compound and its further elaboration to the α , β -unsaturated aldehyde.[11] In the second route (CHART I.B.6.b) the α , β -unsaturated aldehyde unit is generated from a precursor aldehyde by an interesting bis-homologation with Li-CH=CH-OEt at -78°. The saturated aldehyde precursor was, in turn prepared by cleavage of a terminal π system with OsO_4-$NaIO_4$. The Wittig procedure permits each of the two fragments involved to play the role of either the aldehyde or the ylid and CHART I.B.2 and CHART I.B.3 illustrate this.

CHART [illegible].6

a. Synthesis of 11-hydroxy undec 2-ene 1-al



b. Synthesis of 11-tetrahydropyranyloxy undec 2-ene 1-al



The switch from the ylid role to the aldehyde one can be brought about by a simple $-CH_2Br \longrightarrow CHO$ transformation. Thus, the same precursor could be re-structured either to the ylid or to the aldehyde, and this aspect is illustrated in CHART I.B.5.b and CHART I.B.5.c.[13,14,16,17] The finding that 1, ω-nonane dicarboxylic acid - and therefore presumably any 1, ω-dicarboxylic acid - could be degraded under the modified Hunsdiecker conditions to the corresponding ω-bromo carboxylic acid is useful. The ω-bromo carboxylic acids or the corresponding esters could be transformed to the ω-aldehydes by oxidation with pyridine N-oxide (CHART I.B.5.b). The Horner-Wittig reaction involving phosphonate as the reagent has also been used in the preparation of codling moth pheromone.[18]

Synthesis of pheromones of the type,

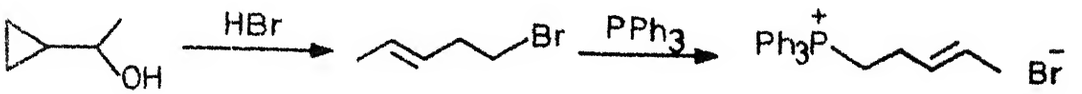
$$CH_3CH\overset{E}{=}CH-CH_2-CH\overset{Z}{=}CH-(CH_2)_8-OAc$$

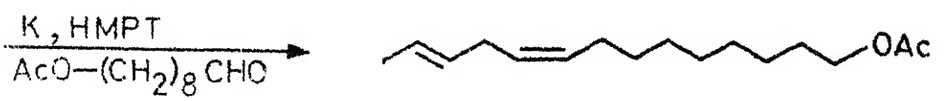
The well known prodenialure belongs to the above type. Surprisingly, thus far, it has been reached, via Wittig reaction by a single route (CHART I.B.7).[19,20] The HBr mediated stereospecific generation of 1-bromo pent(E)3-ene - a synthon used in the Wittig reaction - from alcohol derived from acetaldehyde and cyclopropyl magnesium bromide is an attractive feature of the above prodenialure synthesis.

CHART 1.B.7

Synthesis of $CH_3-CH\overset{E}{=}CH-CH_2-CH\overset{Z}{=}CH-(CH_2)_8-OAc$

by Wittig reaction





Synthesis of insect sex pheromones via coupling of organometallic agents

The union of the two partners, which is the usual strategy for the synthesis of insect sex pheromones (CHART I.B.1), has been brought about by an organometallic compound on the one hand and a halide or equivalent on the other. Although this strategy is of recent origin, the procedure has become popular. The new C-C bond can be generated either with vinyl Grignard reagents with very good stereoselectivity or with other Grignard reagents using catalysts such as $P(OEt)_3$ or $Pd(PPh_3)_4$. Alternately, organometallic compounds from saturated substrates can be coupled effectively with Li_2CuCl_4. Such procedures have an advantage over the Wittig reaction, since the conditions are mild and isolation of products simple.

Synthesis of pheromones of the type,

$$H_3C-(CH_2)_m-CH\overset{Z}{=}CH-(CH_2)_n-OAc$$

CHART I.B.8 illustrates the synthesis of insect sex pheromones possessing a single π bond, by coupling involving organometallic agents. Insect sex pheromone relating to Paralobesia viteana has been prepared with exceptional stereochemical purity by the coupling of $\left[\underline{E}t-CH\overset{Z}{=}CH\right]_2$ CuLi - prepared from Et_2CuLi and acetylene - with 1-acetoxy 8-iodo octane.[21] The synthesis of Spodoptera frugiperda pheromone from 8-tetrahydropyranyloxy octyl magnesium bromide and 1-iodo hex (Z) 1-ene[23]

CHART 1.B.8

Synthesis of Pheromones of the type,

$CH_3-(CH_2)_m-CH\overset{Z}{=}CH(CH_2)_n-OAc$ by Organometallic coupling

Ref.	Organometallic compound	Coupling partner	Conditions
21	$\left[H_3C-CH_2-CH\overset{Z}{=}CH\right]_2CuLi$	$I-(CH_2)_8-OAc$	THF/HMPT/$P(OEt)_3$
22	$H_3CCH_2-CH\overset{Z}{=}CH-(CH_2)_2MgBr$	$I-(CH_2)_6OTHP$	Not given
23	$THPO-(CH_2)_8-MgBr$	$I-CH\overset{Z}{=}CH-(CH_2)_3CH_3$	$Pd(PPh_3)_4$
24	$H_3C-(CH_2)_3-CH\overset{Z}{=}CH-(CH_2)_3MgBr$	$Br-(CH_2)_n-OAc$ n = 5,7	Li_2CuCl_4, 10°-15°

deserves special mention. The highlight of this route is the direct transformation of an organoborane to the corresponding Grignard reagent by exchange with $BrMg(CH_2)_5MgBr$ (CHART I.B.9.a) This $\pi \longrightarrow$ organoborane $\longrightarrow$ Grignard reagent route appears to be superior to alternate procedures, such as, anti-Markownikof HBr addition followed by Mg treatment. Further, the synthetic strategy which neatly sandwiches a Cu^{I} mediated coupling between two organoborane $\longrightarrow$ Grignard reagent changes (CHART I.B.9.a) is appealing. The isomeric purity is also high.

1-Methyl cycloocta 1,5-diene arising from 1,3-butadiene and 2-methyl 1,3-butadiene is the surprising precursor to non (Z) 4-enyl magnesium bromide[24] (CHART I.B.9.b). The latter, for example, is transformed to Mamestra configurata pheromone on coupling with 7-acetoxy 1-bromo heptane, which, amusingly, has been prepared from cyclo-octene[24] (CHART I.B.9.c)!

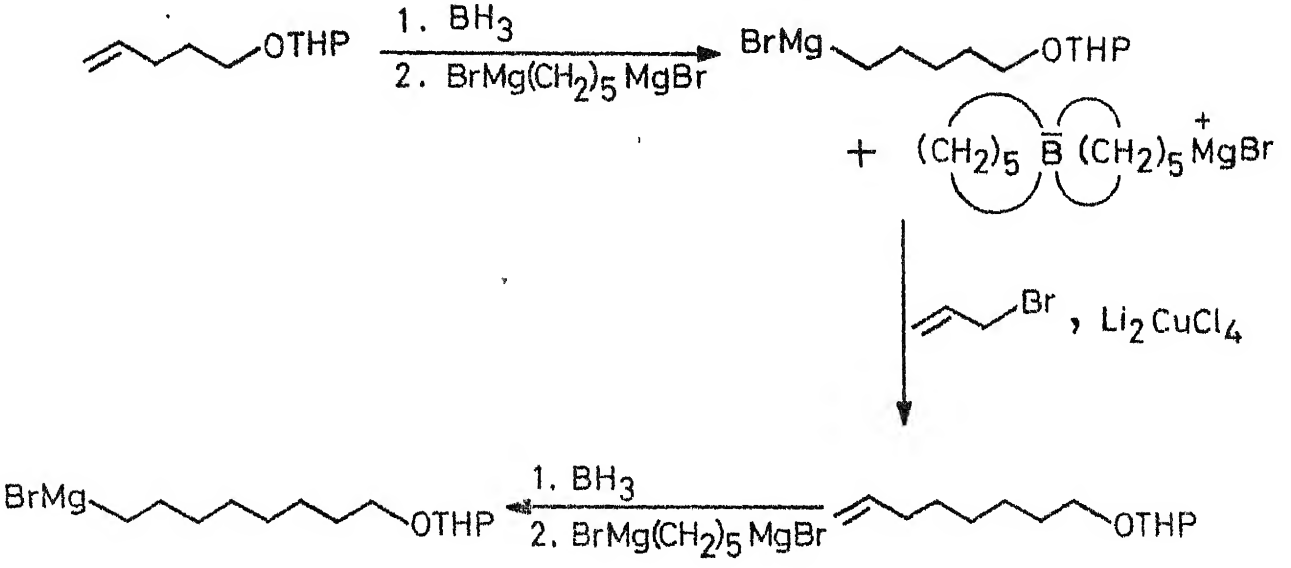
Synthesis of pheromones of the type,

$$H-(CH_2)_m-CH\overset{E}{=}CH-CH\overset{E}{=}CH-(CH_2)_n-OH$$

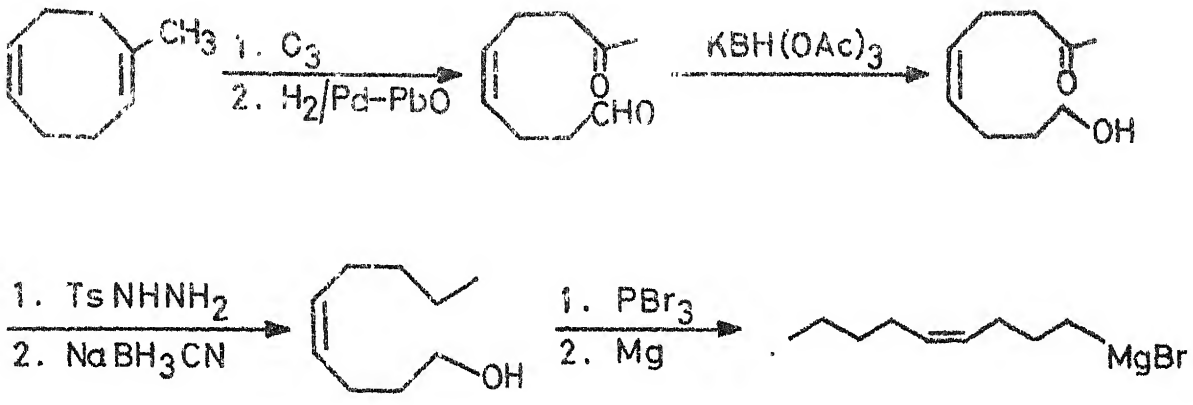
The endeavours in this category are largely related to the synthesis of the codling moth pheromone, $CH_3-CH=CH-CH=CH-(CH_2)_7-OH$ and invariably the strategy involves C-C coupling wherein the hydrophobic tail fragment already possesses the required E,E-stereochemistry (CHART I.B.10). The readily available sorbic acid $H_3C-CH=CH-CH=CH-COOH$ naturally turns out to be the most

CHART 1.B.9

a. Synthesis of 8-tetrahydropyranyloxy octyl magnesium bromide



b. Synthesis of 2-non 4-enyl magnesium bromide



C. Synthesis of 7-acetoxy 1-bromoheptane

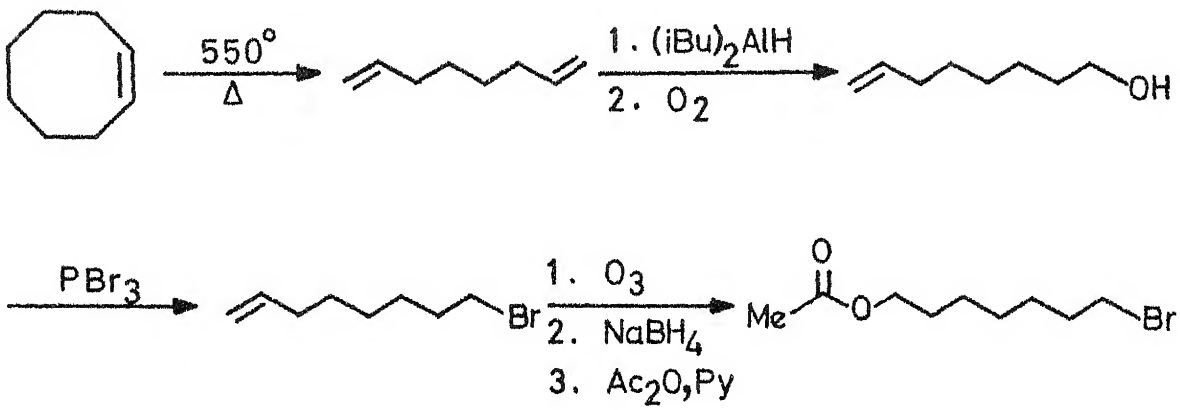


CHART 1.B.10

Synthesis of pheromones of the type:

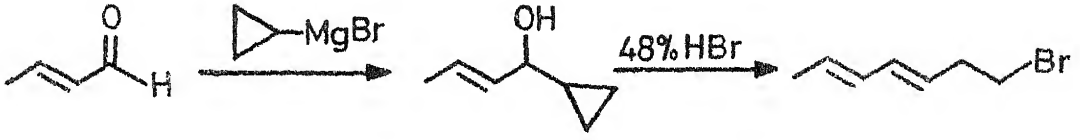
$H-(CH_2)_m-CH\overset{E}{=}CH-CH\overset{E}{=}CH-(CH_2)_n-OAc$ by organometallic coupling

Ref.	Organometallic compound	Coupling partner	Conditions
25-28	$RO-(CH_2)_5-MgX$ R = –Si– or  ; X = Cl or Br	$Br-(CH_2)_2-CH\overset{E}{=}CH-CH\overset{E}{=}CHCH_3$	THF, Cu^+, –5°
29-30	$THPO(CH_2)_6-MgBr$	$Br-CH_2-CH\overset{E}{=}CH-CH\overset{E}{=}CHCH_3$	Li_2CuCl_4, –15°
31-32	$THPO(CH_2)_6-MgBr$	$AcO-CH_2-CH\overset{E}{=}CH-CH\overset{E}{=}CHCH_3$	Li_2CuCl_4, –15°
33	$Me_3SiO-(CH_2)_6-MgBr$	$Br-CH_2-CH\overset{E}{=}CH-CH\overset{E}{=}CHCH_3$	CuCl, –5°–10°
34	$Me_3SiO(CH_2)_5-MgBr$	$BrCH_2CH_2-CH\overset{E}{=}CH-CH\overset{E}{=}CHCH_3$	Li_2CuCl_4, –5°–0°
35	$THPO-(CH_2)_6-MgCl$	$I^-Me_3N^+-CH_2-CH\overset{E}{=}CH-CH\overset{E}{=}CHCH_3$	Li_2CuCl_4
36	$THPO-(CH_2)_n-MgBr$ n = 6, 7	$Br-CH_2-CH\overset{E}{=}CH-CH\overset{E}{=}CH-(CH_2)_mH$ m = 0, 1	THF–HMPA
37	$THPO-(CH_2)_4-MgCl$	$I-(CH_2)_5-CH\overset{E}{=}CH-CH_2OPh$	CuI, 

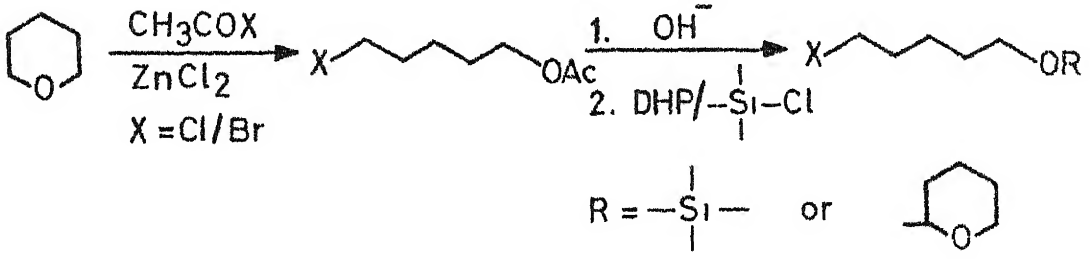
commonly used starting material for this purpose. However, the notable exceptions are the use of $H_3C-CH\overset{E}{=}CH-CH\overset{E}{=}CH-CH_2CH_2Br$, generated stereospecifically from the cyclopropyl magnesium bromide - crotonaldehyde adduct with HBr (CHART I.B.11.a)[25,26,28] and the quite unconventional $H_3C-CH\overset{E}{=}CH-CH\overset{E}{=}CH-CH_2\overset{+}{N}Me_3I^-$ prepared from an even more unconventional starting material, namely, 2-picoline.[35] (CHART I.B.11.c) The former arises from reduction of an iminium ion, which, in turn, is generated by removal of elements of water from a protonated N-oxide (CHART I.B.11.C). The hydrophilic head fragments are usually derivatives of 1, ω-halohydrins and in some cases are formed from cyclic ethers[25,27] (CHART I.B.11.b and CHART I.B.11.d). The coupling is efficiently catalysed by Cu^I species, which are directly introduced as CuCl, CuI or are formed <u>in situ</u> from Li_2CuCl_4. Generally, the coupling proceeds with good retention of stereoselectivity and the yields are in the range of 75-80%. The synthesis of bollworm moth pheromone, $H_2C=CH-CH\overset{E}{=}CH-(CH_2)_8-OAc$ from 1,3-butadiene[37] is noteworthy (CHART I.B.11.e), since, it has several novel features. The 2,7-octadiene unit arising from Pd mediated dimerization of butadiene in the presence of phenol has been specifically subjected to hydroboration - oxidation at the terminal π. The resulting alcohol is transformed to iodide and coupled with C_4 Grignard arising from THF. The resulting monoene is transformed to the desired diene by a Pd^{II} mediated removal of elements of phenol. Thus the phenol introduced in the first stage is removed in the final one.

CHART 1.B.11

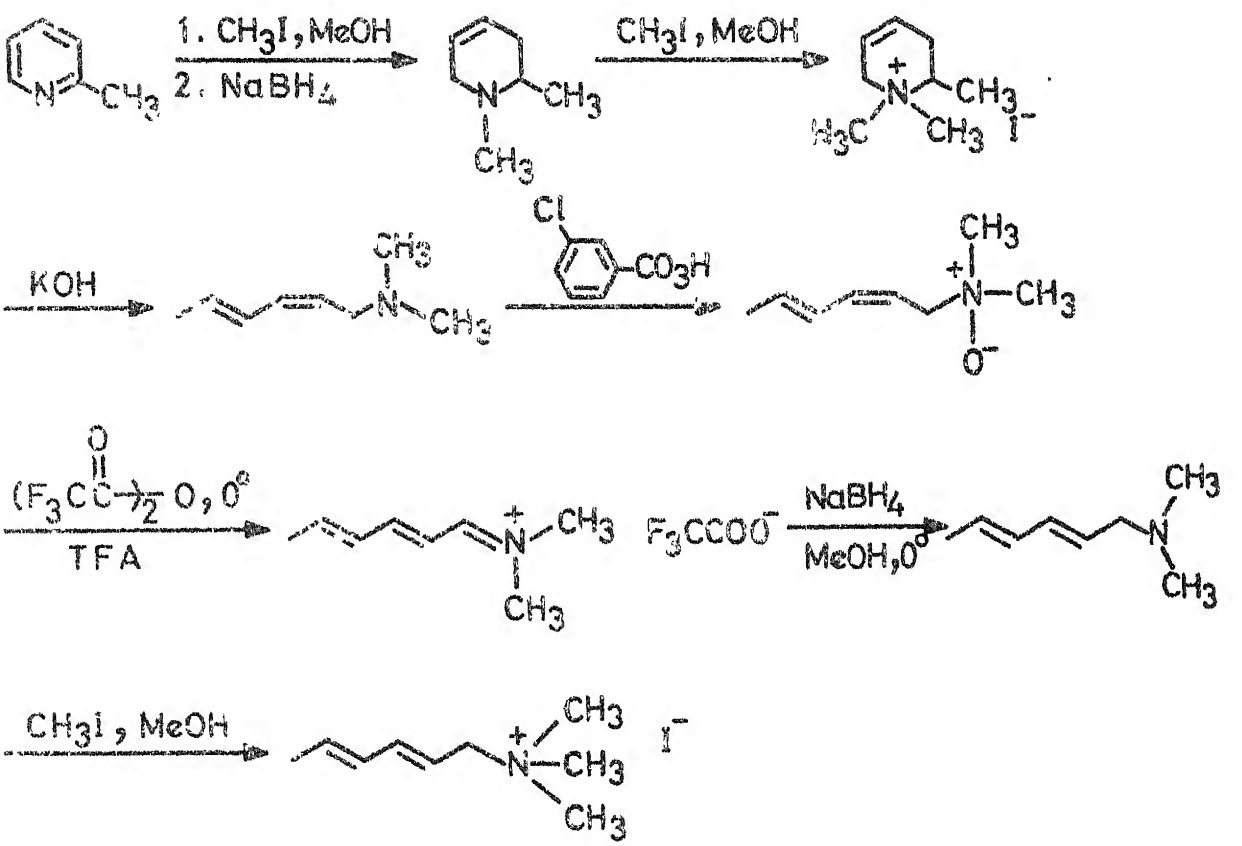
a. Synthesis of 1-Bromohepta E,E-3,5-diene



b. Synthesis of O-protected 1-halopentan 5-ol

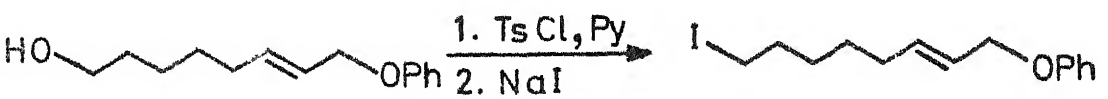


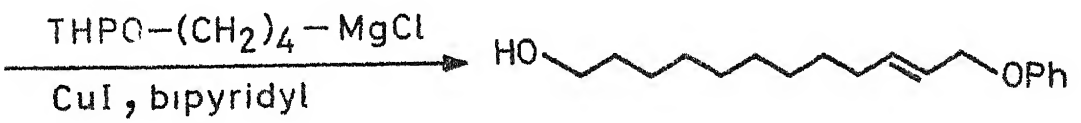
C. Synthesis of 1-N,N,N-trimethylammonium hexa-E,E-3,5 diene iodide.

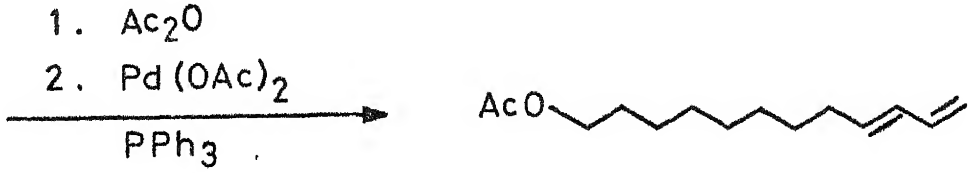


d. Synthesis of 4-tetrahydropyranyloxybutyl magnesium chloride

e. Synthesis of 1-acetoxydodeca E-9,11 diene.







Synthesis of insect sex pheromones *via* organometallic agent - carbonyl addition

The codling moth pheromone, CH_3-CH=CH-CH=CH-$(CH_2)_7$-OH has been prepared by addition of C-6 organometallic agent to either sorbic acid or to the corresponding aldehyde.[38,39,40,41] In the former case the resulting dienone - dienol change was brought about with AlH_3. In both cases the hydroxyl group was removed *via* mesylate reduction (CHART I.B.12).

Synthesis of insect sex-pheromones by acetylide coupling

The union of the hydrophilic head group with the hydrophobic rear section is possible by displacement of a leaving group with acetylide anion. The resulting substituted acetylene can be transformed selectively either to the E or the Z olefin. Although this procedure is perhaps the oldest with reference to the synthesis of pheromones, it still enjoys wide application, particularly with regards to large scale synthesis. The method suffers from disadvantages such as, difficulty in the formation of acetylides having long methylene chains, incomplete alkylation and the rather particular controls that are required to achieve maximum stereoselectivity.

Pheromones, of relevance to the present work, that have been prepared from acetylene precursors are presented in CHART I.B.13 and CHART I.B.14. The acetylene unit has been

CHART I.B.12

Synthesis of the pheromone dodeca E,E-8,10 dien 1-ol

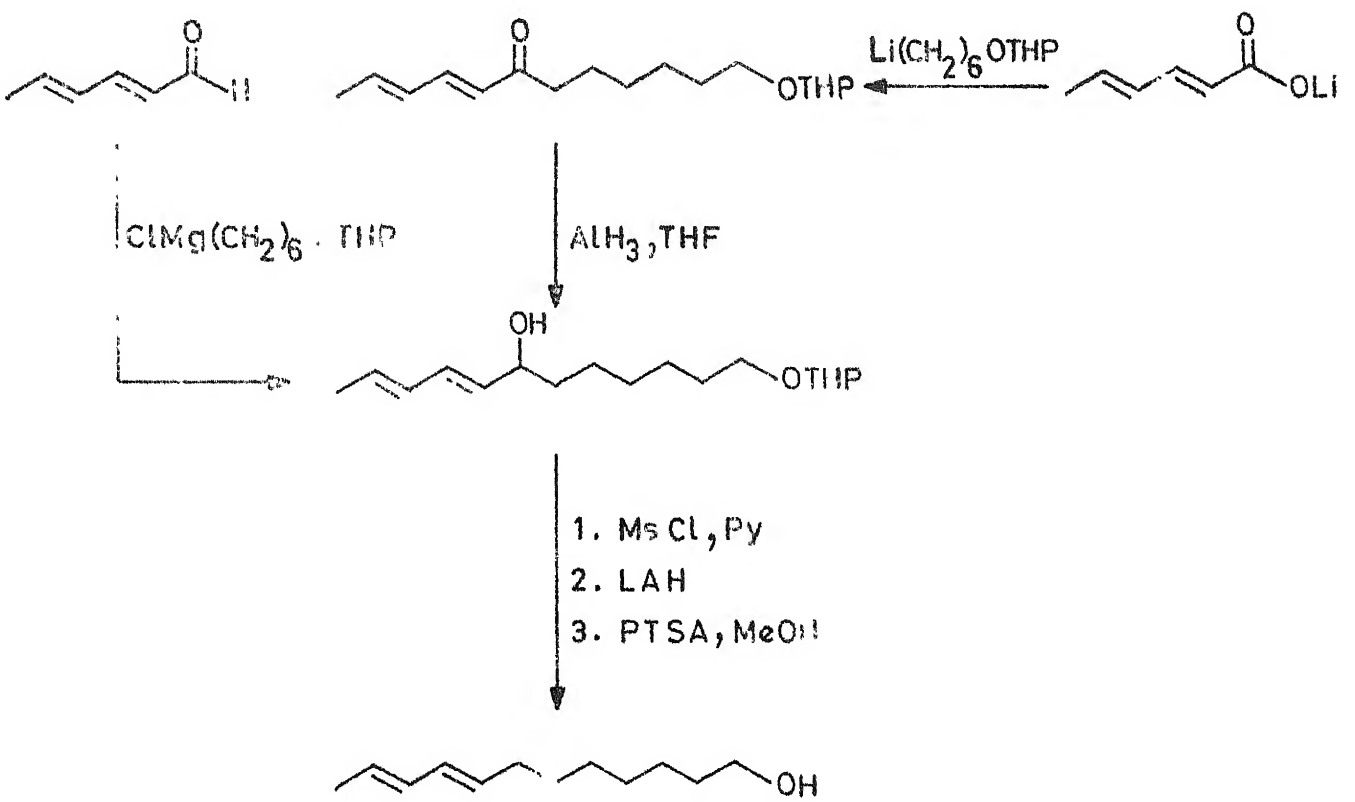


CHART I.B.13

Synthesis of pheromones of the type,

$CH_3(CH_2)_m-CH\overset{Z}{=}CH-(CH_2)_n-OAc$ by acetylide coupling

Ref.	Acetylene	Coupling partner	Coupling conditions
42	$THFO-(CH_2)_n-C\equiv C-H$ n = 8,10	$Br-(CH_2)_m-CH_3$ m = 3,5	n-BuLi, THF-HMPT
43	$THPO-(CH_2)_8-Br$ + $Li-C\equiv C-H$ (DMSO, EDA)	$Br-Et$	$LiNH_2$
44	$THPO-(CH_2)_8-Cl$ + $Li-C\equiv C-H$ (DMSO)	$Br-(CH_2)_3-CH_3$	$NaNH_2$
45	$CH_3(CH_2)_m-C\equiv C-H$ m = 0,2,3,5	$Cl-(CH_2)_n-OTHP$ n = 4,6,8,9,10	Not given

CHART 1.B.14

Synthesis of pheromone $H_3C-CH\overset{E}{=}CH-CH_2-CH\overset{Z}{=}CH-(CH_2)_8-OAc$ by acetylide coupling

Ref.	Acetylene	Coupling partner	Conditions
45	$THPO-(CH_2)_8-C\equiv C-H$	$Cl-CH_2-CH\overset{E}{=}CH-CH_3$	Not given
46	$THPO-(CH_2)_8\ Cl$ + $Li-C\equiv C-H$ (DMSO)	$Br-CH_2-CH\overset{E}{=}CH-CH_3$	$LiNH_2$, dioxane
47	$K=CH-(CH_2)_7-C\equiv C-H$ ($K=-O-CH_2-CH_2-O-$)	$Br-CH_2-CH\overset{E}{=}CH-CH_3$	$LiNH_2$, dioxane

used as a connector of the two segments by sequential alkylation initiated with lithium acetylide. The pheromone prodenialure is invariably made by acetylide alkylation with crotyl halides.

The synthesis of insect sex pheromones by atypical procedures

Codling moth pheromone, $CH_3-CH\overset{E}{=}CH-CH\overset{E}{=}CH-(CH_2)_7-OH$, has been prepared by sequential alkylation using 3-oxo glutarate. The 3-oxo glutarate system $E-CH_2-CO-CH_2-E(E=COOEt)$ possesses two equivalent active positions and the synthetic strategy involves attachment of the hydrophobic tail unit to one and then the hydrophilic head unit to the other ! The resulting bis keto ester system leads to ketone from loss of elements of CO_2 whose tosylhydrazone is then reduced with $NaBH_3CN$ [48] (CHART I.B.15) !

The transformation of cyclododeca E,Z-1,3-diene to boll-worm moth pheromone (CHART I.B.16) constitutes, above all, an impressive display of modern synthetic reagents and reactions ! Thus the Z π bond is selectively cleaved with OSO_4-NaIO_4, reduced to alcohol at one end and E-allylic alcohol at the other, the bond epoxidized with $V(AcAc)_3$-t-BuOOH, the hydroxyl ends protected with Me_3SiCl, the epoxide stereoselectively opened with diethyl-aluminium tetramethyl piperidide to π shifted allyl alcohol, the end protection removed with KF, the vic diol of the resulting triol protected as acetonide, the remaining hydroxyl acetylated, the vic diol protection removed, the resulting glycol transformed

CHART 1.B.15

Preparation of $CH_3-CH=^{E}CH-CH=^{E}CH-(CH_2)_7-OH$ by oxo glutarate alkylation

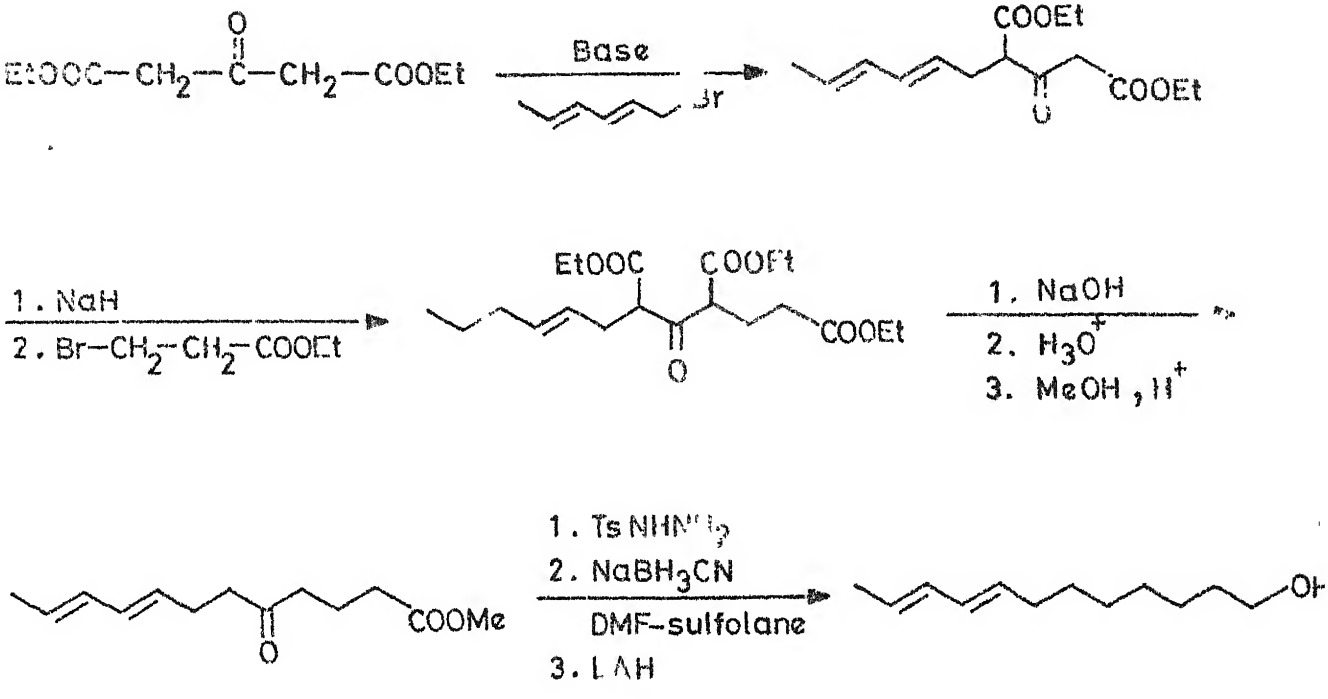
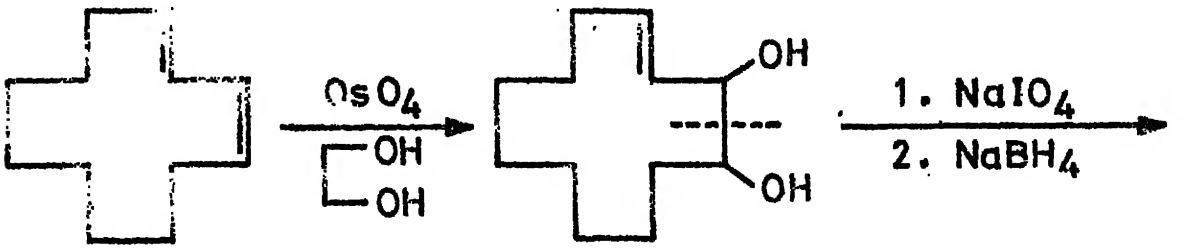
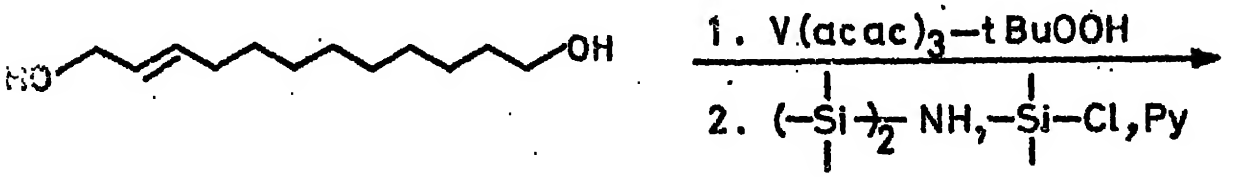
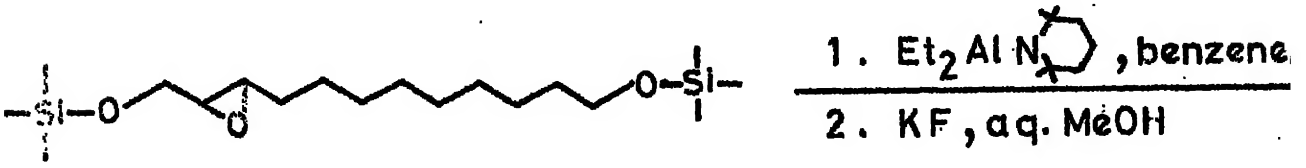


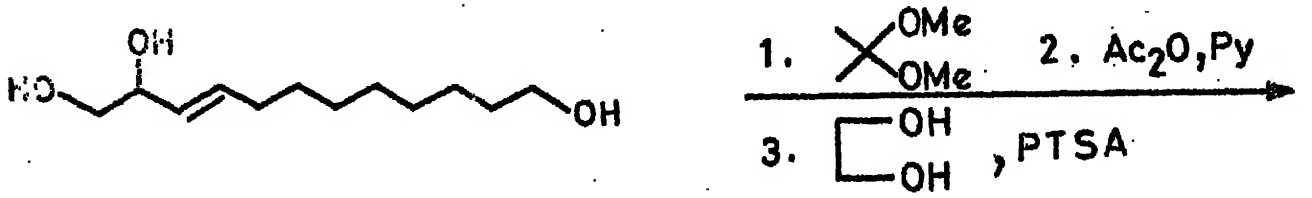
CHART 1.B.16

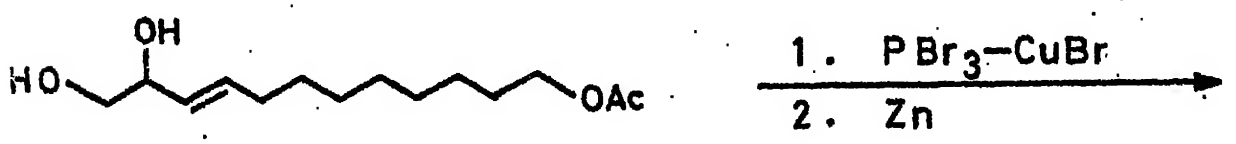
Synthesis of $H_2C{=}CH{-}CH{\overset{E}{=}}CH{-}(CH_2)_8{-}OAc$ from cyclododeca E,Z-1,3-diene

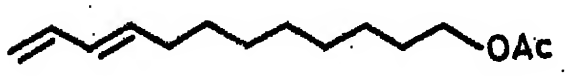










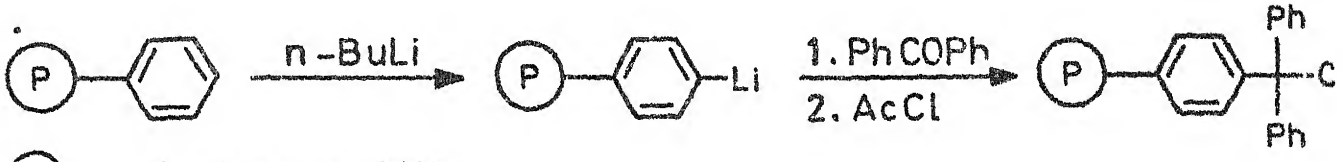


to dibromide with PBr_3-CuBr and then transformed to terminal π with zinc !.[49] This appears to be a tough way to reach the pheromone but certainly illustrates the power of current organic synthetic methodology.

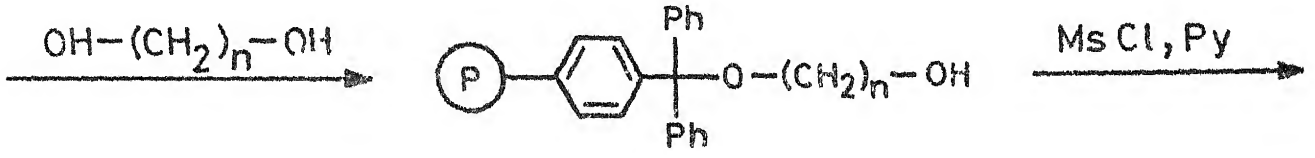
A variation of the acetylide alkylation has been achieved with the hydrophilic head fragments implanted on a polymer suppo Elements of tritylchloride moiety are attached to phenyl groups of a polystyrene - divinyl benzene co-polymer which when reacted with symmetrical 1, ω-diol leads to the mono O-protected entity. The resulting alcohol is activated as mesylate and used to alkylate the acetylide. The resulting di-substituted acetylene is partially hydrogenated and the polymer freed with acid as polymer bound trityl alcohol. The pheromone synthesis is completed by acetylation (CHART I.B.17).[50-52]

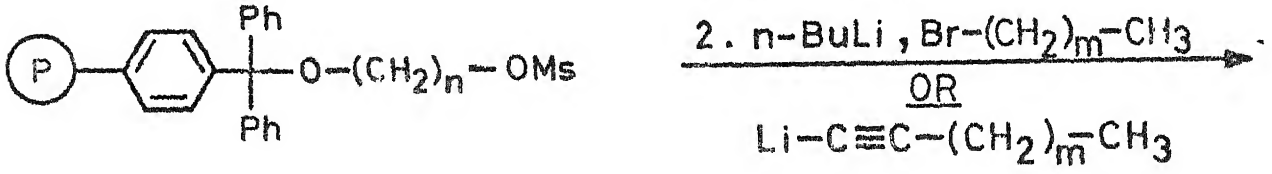
CHART 1.B.17

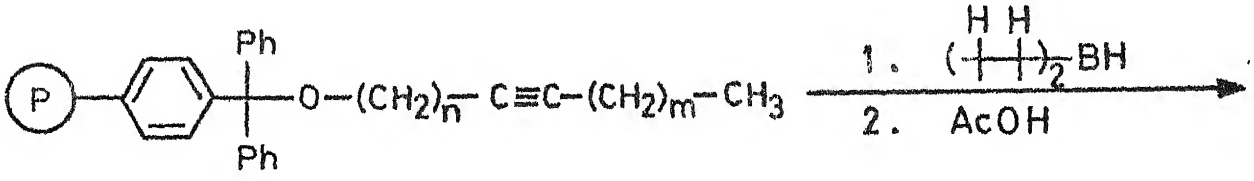
Synthesis of pheromones on polymer support

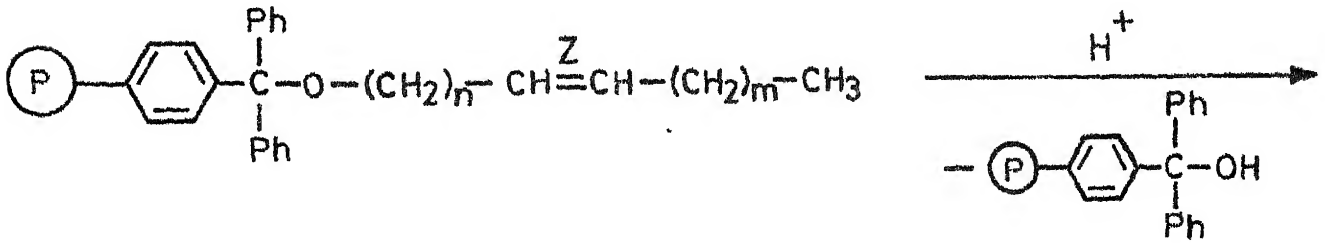


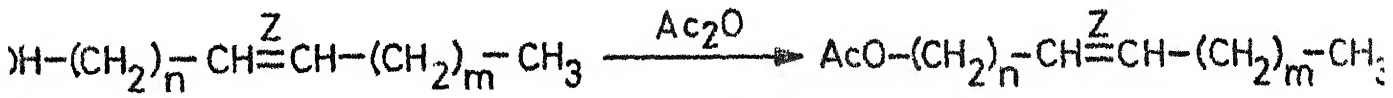
(P) = polystyrene-DVB polymer backbone











n = 6,8,10 m = 1,3

I.C. PRESENT WORK

An account pertaining to the appropriateness of the present work has been provided in SECTION I.A.

The current focus in the use of small molecules, that are so effectively used, in communication, courtship and social behaviour by practically every member of the vast insect domain has, *inter alia*, led to a resurgence of interest in naturally occurring aliphatic carbon frameworks. Fatty acids, endowed as they are with a wide spectrum of functional group arrays are principal beneficiaries of this welcome trend. Even amongst these, Indian castor oil stands out as an exceptionally versatile substrate. Most fatty acids are present, at the source, in the company of closely related structures and therefore their isolation in pure state poses problems. Castor oil, which contains 91-93% of the triglycerol ester of ricinoleic acid, is, indeed, a rare exception. Yet another attractive feature in castor oil is the presence of the unusual γ, δ-unsaturated alcohol unit which is the focal point of reactivity in the molecule.

Consequently, it was felt that castor oil would be a good substrate for the illustration of a new facet in the art of organic synthesis, namely, the transformation of rare natural

products of current interest and utility. The transformation of castor oil ⟶ insect sex pheromones, presented in this section, is the outcome of such an analysis. The practical, as well as challenging, aspects of such transformations were also an important consideration. In most cases, synthesis by Man cannot compete with that of Nature and therefore a great many of the laboratory synthesis of natural products, although of immense significance in the understanding of bond-forming and bond-breaking interactions relating to carbon substrates, have little direct practical utility. This is not the case with insect sex pheromones, which are so thinly spread amongst vast sexually specific insect populations, that their isolation from natural sources is an impractical proposition. On the other hand, their preparation in the laboratory is also not without problems. The simple structures of insect sex pheromones, belie the ardours associated with their synthesis. Indeed, endowed as they generally are, on a linear carbon backbone, with terminal functional groups and stereochemically specific π , multiple π and skipped π arrays, pose sufficient strategic and experimental challenges. The present work is no exception, and was beset with a very generous measure of problems in the initial stages.

In the present work, castor oil has been transformed to the pheromones listed in CHART I.A.1 (page 3). Amongst these the pheromones related to Bombus lucorum and Heliothis virescens

have not been synthesised thus far. In almost all cases the stereochemical purity is equal to or better than that reported from earlier synthetic endeavours (SECTION I.B). Pheromones made by each of the two major routes (vide infra) have been analysed by Dr. David Hall, Tropical Products Institute, London, England,on 1.8 m x 2 mm i.d. 5% SE 30/0.5% 20 M on chromosorb W HP, 1.8 m x 2 mm i.d. 1.5% carbowax 20 M on chromosorb G, and 1.8 m x 2 mm i.d. 5% 4-(p-methoxycinnamyloxy)-4'-methoxyazobenzene on Gas Chrom Q columns, for whose painstaking interest in our work we are most grateful.

Pheromones possessing exclusive E configuration have been prepared from appropriate oxo synthons derived from castor oil via Wittig reaction and those possessing either Z or E,Z configuration by acetylide coupling.

The oxo synthons were generally prepared by pathways delineated from earlier work in our laboratories.[53] However, considerable improvements have been made in several of the key steps and experimental procedures standardised by repeated trials. The C-10 acetylide synthon, precursor to a host of insect sex pheromones, is a novel one. The C-11 acetylide synthon served, not only as an excellent substrate for model studies, but also has been transformed to insect sex pheromone relating to Archips semiferanus.

The preparation of oxo synthons, methyl 11-oxo (E) 9-undecenoate (7) and methyl 10-oxo (E) 8-decenoate (15)

Castor oil was transformed to methyl ricinoleate (1) in 85% yields by trans-esterification with methanol containing small amounts of sodium methoxide. The $\pi^2 s + \sigma^2 s + \sigma^2 s$ fragmentation to methyl 10-undecenoate (2) and heptaldehyde (3) was accomplished in 49% yields by thermolysis of 1, evenly supported either on glass-wool or sand. The methyl 10-undecenoate (2) to methyl 9-decenoate (11) change was carried out via PhMgBr addition to alcohol 8, thermal dehydration to diene 9, chromic acid oxidation to acid 10 and Fischer esterification (CHART I.C.1).

---

1 : bp 128-30°/0.02 torr;

ir : ν_{max}(neat) (cm^{-1}): 3570 (hydroxyl), 1740 (ester).

nmr: $\delta_{(CDCl_3)}$: 3.65(s,3H,-COOC$\underline{H}_3$), 5.45 (m, 2H, olefinic).

2 : bp 80-81°/0.09 torr;

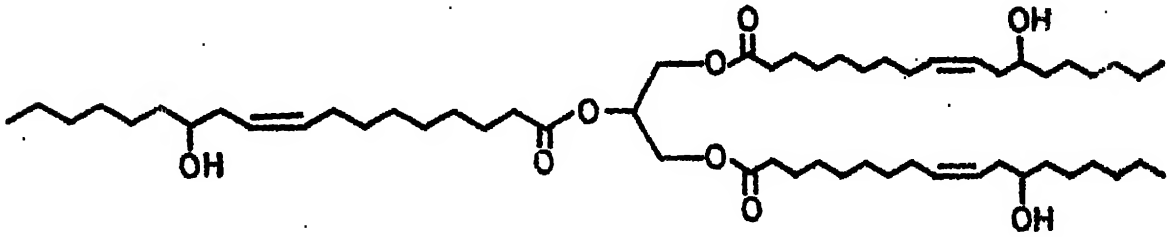
ir : ν_{max}(neat) (cm^{-1}): 1740 (ester), 1655 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.65 (s, 3H, -COOC$\underline{H}_3$), 5.0 (m, 2H, olefinic), 5.8 (m, 1H, olefinic).

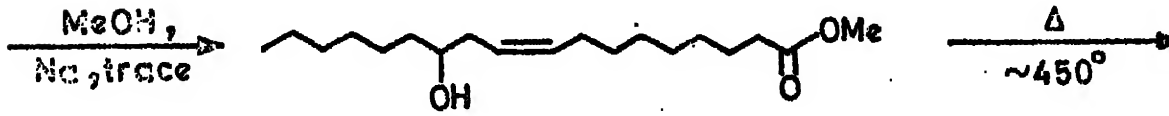
8 : ir : ν_{max}(neat) (cm^{-1}): 3595 (hydroxyl), 1655 (double bond), 1610 (phenyl).

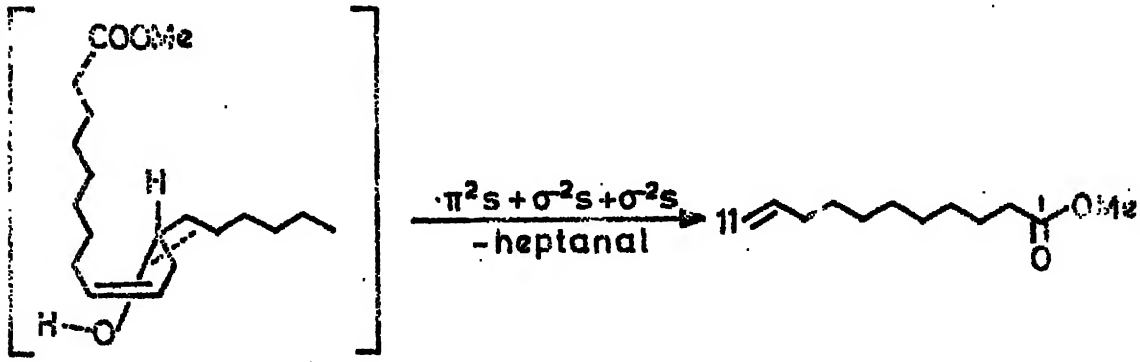
CHART I.C.1

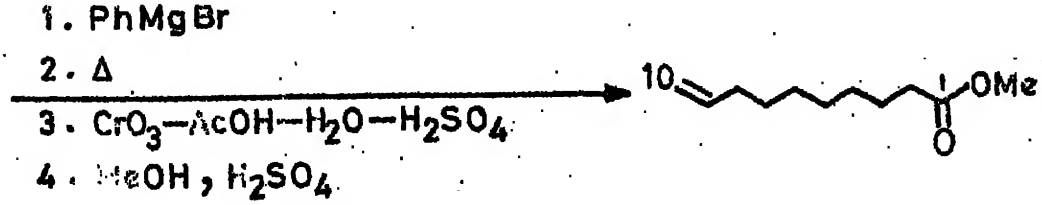
Transformation of Castor oil to methyl undec 10-enoate (2) and methyl dec 9-enoate (11)



castor oil







9 : bp 163-165°/0.07 torr;

ir : ν_{max}(neat)(cm^{-1}): 1655 (double bond), 1610 (phenyl).

nmr: $\delta_{(CDCl_3)}$: 5.0 (m, 2H, olefinic), 5.85 (m, 1H, olefini
7.2 (m, aromatic).

10: bp 93-95°/0.8 torr;

ir : ν_{max}(neat)(cm^{-1}): 1710 (carboxyl), 1655 (double bond)

nmr: $\delta_{(CDCl_3)}$: 5.0 (m, 2H, olefinic), 5.8 (m, 1H, olefinic)

11: bp 60-61°/0.3 torr;

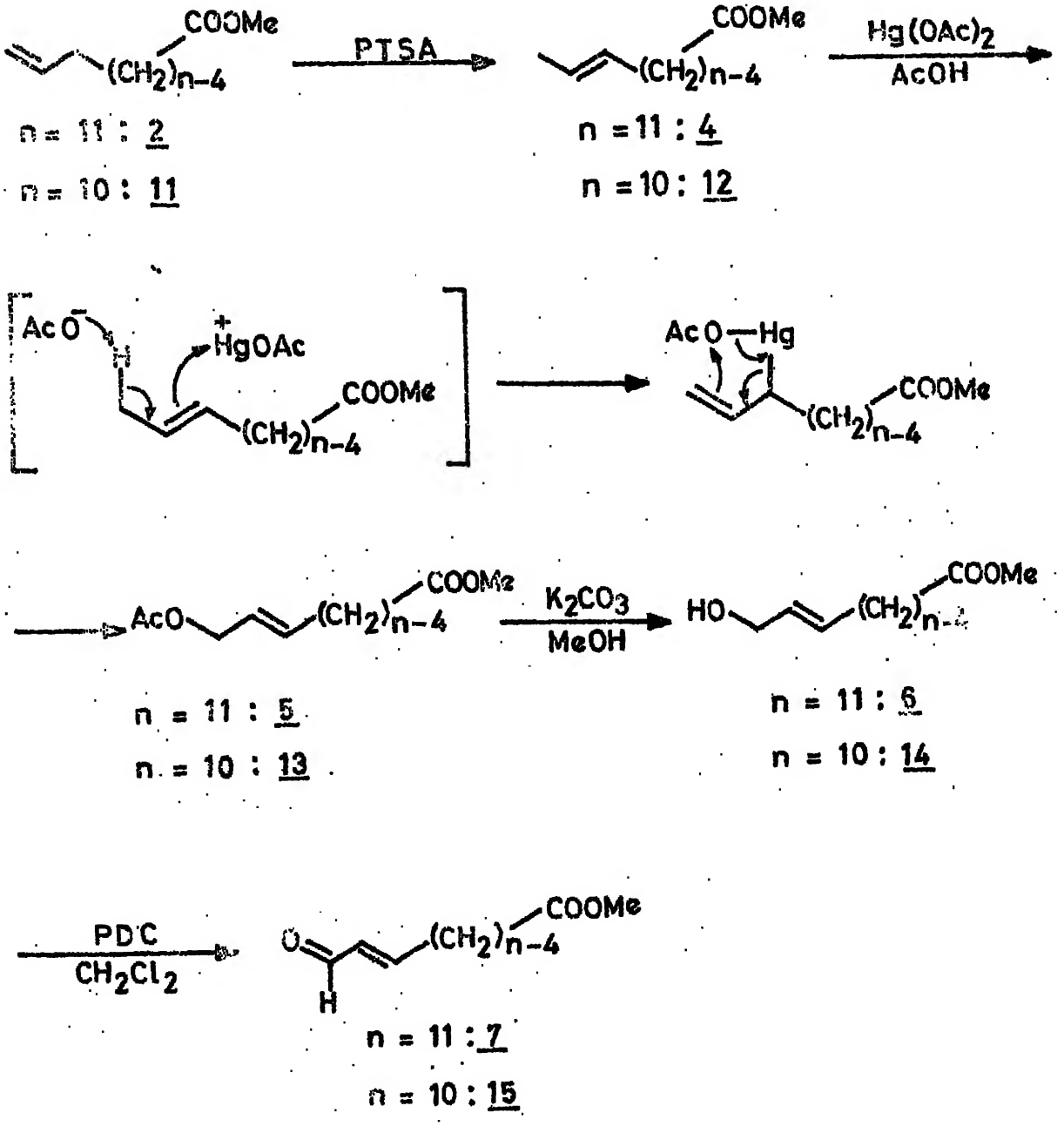
ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1655 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.68 (s, 3H, $-COOCH_3$), 4.9 (m, 2H, olefinic)
5.8 (m, 1H, olefinic).

Methyl 10-undecenoate (2) and methyl 9-decenoate (11) were isomerised in refluxing benzene containing PTSA to methyl (E) 9-undecenoate (4) (96%) and methyl (E) 8-decenoate (12) (97%), and then regioselectively acetoxylated with $Hg(OAc)_2$-AcOH to, respectively, methyl 11-acetoxy (E) 9-undecenoate (5) (86%) and methyl 10-acetoxy (E) 8-decenoate (13) (85%) (CHART I.C.2). The allylic acetates 5 and 13 thus obtained were converted by trans-esterification with K_2CO_3-MeOH to allylic alcohols 6 (92%) and 14 (94%) and then oxidised with PDC-CH_2Cl_2, in vastly

CHART I.C.2

Preparation of synthons, 11-oxo undec E-9-enoate (7) and 10-oxo dec E-8-enoate (15)



n = 11 : 2
n = 10 : 11

n = 11 : 4
n = 10 : 12

n = 11 : 5
n = 10 : 13

n = 11 : 6
n = 10 : 14

n = 11 : 7
n = 10 : 15

enhanced yields, to the key oxo synthons, methyl 11-oxo (E) 9-undecenoate (7) (84%) and methyl 10-oxo (E) 8-decenoate (15) (82%) (CHART I.C.2). Thus, in the present work, the most practical routes to synthons 7 and 15 have been presented. Parenthetically, compound 15 has been recognized, recently, by other groups also as an important synthon.[54]

---

4 : bp 79-80°/0.8 torr

ir : ν_{max}(neat) (cm^{-1}): 1740 (ester), 1640, 970 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.65 (s, 3H, $-COOCH_3$), 5.4 (m, 2H, olefinic).

12: bp 60-61°/0.2 torr

ir : ν_{max}(neat) (cm^{-1}): 1740 (ester), 1640, 970 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.65 (s, 3H, $-COOCH_3$), 5.4 (m, 2H, olefinic).

5 : bp 115°/0.2 torr

ir : ν_{max}(neat) (cm^{-1}): 1740 (ester), 1730 (acetate).

nmr: $\delta_{(CDCl_3)}$: 2.0 (s, 3H, $-OCOCH_3$), 3.65 (s, 3H, $-COOCH_3$), 4.5 (d, J=5Hz, 2H, $-CH_2-OAc$), 5.65 (m, 2H, olefinic).

13: bp 115°/0.13 torr

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1730 (acetate).

nmr: $\delta_{(CDCl_3)}$: 2.0 (s, 3H, $-OCOCH_3$), 3.65 (s, 3H, $-COOCH_3$), 4.5 (d, J=5Hz, 2H, $-CH_2OAc$), 5.65 (m, 2H, olefinic).

6 : bp 120-121°/0.07 torr

ir : ν_{max}(neat)(cm^{-1}): 3640 (hydroxyl), 1740 (ester).

nmr: $\delta_{(CDCl_3)}$: 3.65 (s, 3H, $-COOCH_3$), 4.0 (br, 2H, $-CH_2-OH$), 5.6 (m, 2H, olefinic).

14: bp 115°/0.04 torr

ir : ν_{max}(neat)(cm^{-1}): 3640 (hydroxyl), 1740 (ester).

nmr: $\delta_{(CDCl_3)}$: 3.65 (s, 3H, $-COOCH_3$), 4.0 (br, 2H, $-CH_2-OH$), 5.65 (m, 2H, olefinic).

7 : bp 105-110°/0.06 torr

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1690 (aldehyde), 1660 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.68 (s, 3H, $-COOCH_3$), 6.1 (m, 1H, olefinic), 6.9 (m, 1H, olefinic), 9.4 (d, J=9Hz, 1H, -CHO).

Semicarbazone: mp 139-140°

ir : ν_{max}(KBr)(cm^{-1}): 3280 (-NH), 1740 (ester), 1695 (amide), 1655 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.75 (s, 3H, $-COOC\underline{H}_3$), 5.8 (br, 2H, olefinic) 6.2 (br, 2H, $-CON\underline{H}_2$), 7.5 (br, 1H, $-N\underline{H}$), 9.9 (br, 1H, $-C\underline{H}=N-$).

15: bp 108-113°/0.1 torr

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1690 (aldehyde), 1640 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.65 (s, 3H, $-COOC\underline{H}_3$), 5.8 (m, 1H, olefinic), 6.75 (m, 1H, olefinic), 9.4 (d, J=9Hz, 1H, $-C\underline{H}O$).

Semicarbazone: mp 130-131°

ir : ν_{max}(KBr)(cm^{-1}): 3280 (-NH), 1740 (ester), 1690 (amide), 1655 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.78 (s, 3H, $-COOC\underline{H}_3$), 5.78 (br, 2H, olefinic), 6.20 (br, 2H, $-CON\underline{H}_2$), 7.50 (br, 1H, $-N\underline{H}$), 9.88 (br, 1H, $-C\underline{H}=N-$).

Synthesis of (E) 9,11-dodecadien 1-ol acetate (18): The pheromone of red bollworm moth

Red bollworm moth is a major cotton pest. The natural pheromone, isolated from female abdominal tips, was found to be a E:Z::80:20 mixture.[55] Interestingly, field trials have demonstrated that the maximum male attraction can be achieved

with a mixture containing at least 90% of the E isomer and acetoxy 11-dodecene in the ratio 4:1.

In the present work, the synthesis of the red bollworm moth pheromone, (E) 9,11-dodecadien 1-ol acetate (18) was accomplished via Wittig reaction on methyl 11-oxo (E) 9-undecenoate (7) with triphenylmethyl phosphorane, to methyl (E) 9,11-dodecadienoate (16) (53%) followed by LAH reduction to alcohol 17 (81%) and acetylation, in quantitative yields, with Ac_2O-pyridine (CHART I.C.3).

16: ir : ν_{max}(neat) (cm^{-1}): 1740 (ester), 1652, 970 (double bond).

nmr: $\delta_{(CCl_4)}$: 1.9-2.5 (m, 4H, $=CH-C\underline{H}_2$, $-C\underline{H}_2COOCH_3$), 3.7 (s, 3H, $-COOC\underline{H}_3$), 4.6-6.6 (complex multiplet, 5H, olefinic).

17: ir : ν_{max}(neat) (cm^{-1}): 3350 (hydroxyl), 1655, 950 (double bond).

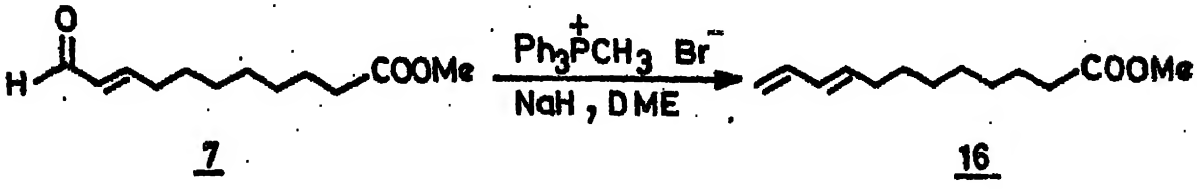
18: bp 105-110°/0.05 torr

ir : ν_{max}(neat) (cm^{-1}): 1740 (ester), 1655, 950 (double bond).

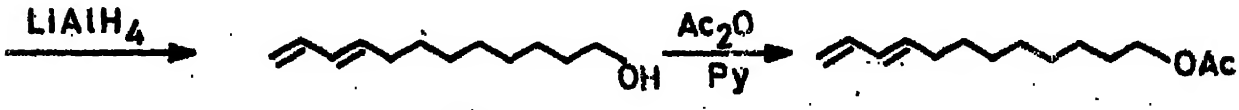
nmr: $\delta_{(CDCl_3)}$: (270 MHz) 2.02 (s, 3H, $-OCOC\underline{H}_3$), 4.06 (t, 2H, $-C\underline{H}_2OAc$), 4.9(dd), 5.2 (dd) ($C\underline{H}_2=CH-$), 5.8 (dt, $-CH=C\underline{H}-CH_2-$), 6.1 (q, $-CH=CH-C\underline{H}=CH-$), 6.3(dt, $H_2C=C\underline{H}-$).

CHART I.C.3

Synthesis of red bollworm moth pheromone (18)



7 16

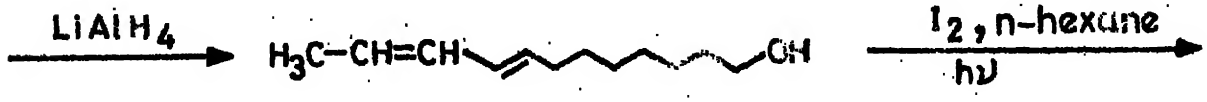


17 18

CHART I.C.4

Synthesis of codling moth pheromone (20)

15 19



20

The isomeric purity of 18 prepared, via sequence outlined, is particularly good, as determined on a (1.8 m x 2 mm i.d) 5% 4-(p-methoxycinnamyloxy)-4'-methoxyazobenzene, on gaschrom Q, 100-120 mesh, column, which showed E:Z::98.7:1.3. Indeed, the present synthesis is the best thus far known to achieve such a high selectivity. In terms of overall yield and availability of synthons the synthesis described here should be the most attractive.

The synthesis of (E,E) 8,10-dodecadien 1-ol (20): The pheromone of codling moth

Codling moth is a major worldwide pest of apple orchards. The pheromone, (E,E) 8,10-dodecadien 1-ol (17) was isolated from virgin females.[56,57] Field trials have established that the pure E,E isomer is far superior to the other three isomers. Indeed, the loss in attractiveness to males on admixture of the E,E with other isomers is due to the fact that the latter are inhibitors !

In the present work, the synthesis of the pheromone of codling moth was achieved by Wittig reaction on methyl 10-oxo (E) 8-dodecenoate (15) leading to, in 50% yields, largely, methyl (E,E) 8,10 dodecadienoate (19), admixed with the (Z,E) isomer. This mixture was reduced to the alcohols (92%) which was

quantitatively isomerised to (E,E) 8,10-dodecadien 1-ol (20) with iodine - n-hexane.[58]

19: ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1655, 970 (double bond).

nmr: $\delta_{(CDCl_3)}$: (270 MHz) 1.65(dd, $C\underline{H}_3$-CH=CH-), 3.65(s, -COO$C\underline{H}_3$), 5.35(dt, -CH=C$\underline{H}$-CH_2-), 5.5(m, CH_3-C$\underline{H}$=CH-), 5.8(m, CH_3-CH=C$\underline{H}$-), 6.3(dd, -C$\underline{H}$=CH-CH_2).

20: ir : ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl), 1655, 970 (double bond).

nmr: $\delta_{(CDCl_3)}$: (270 MHz) [illegible]H), 1.7(dd, $C\underline{H}_3$-CH=CH-), 3.6(t, -$C\underline{H}_2$-OH), 5.35(dt, -CH=C$\underline{H}$-CH_2), 5.6(m, CH_3-C$\underline{H}$=CH-), 6.0(m, CH_3-CH=C$\underline{H}$-), 6.32(dd, -CH=CH-C$\underline{H}$=CH-CH_2-).

There is a tremendous world-wide interest in the codling moth pheromone and the very many syntheses leading to this (SECTION I.B)are a manifestation of the phenomenon. The ready availability of synthon 15 from castor oil, coupled with the only few high yield operations needed further to the pheromone, makes our route to (E,E) 8,10-dodecadien 1-ol as a very attractive one, to eliminate the bothersome apple orchard pest, codling moth.

Preparation of key acetylenic synthons, 1-tetrahydropyranyloxy 10-undecyne (25) and 1-tetrahydropyranyloxy 9-decyne (36)

The genesis of the present work is the realization that a host of insect sex pheromones can arise from 10-undecynoic acid and 9-decynoic acid by, *inter alia*, the key attachment of the hydrophobic tail segments *via* acetylenic coupling. Castor oil could be related to these acetylenic synthons by further transformation of its fragmentation product, methyl 10-undecenoate.

Methyl 10-undecenoate (2) and 9-decenoic acid were readily transformed to the dibromides 21 and 32 with Br_2-CCl_4 in quantitative yields. The crude dibromides were directly converted to the terminal acetylenes with aqueous KOH. This constitutes a very useful procedure, since, generally, such eliminations leading to terminal acetylenes are brought about with sodium-liquid ammonia. In the present work, by carefully monitoring the reaction conditions, it has been possible to obtain even higher yields of terminal acetylenes by this simple procedure, which obviates the use of Na-liquid ammonia. The latter is much less convenient, particularly in the preparation of substantial amounts of terminal acetylenes, required generally as starting materials. Thus, the crude dibromides 21 and 32 on treatment with aqueous KOH at 150-160^{o} for 8 hr gave 10-undecynoic acid (22) (53%) and 9-decynoic acid (33) (78%). The

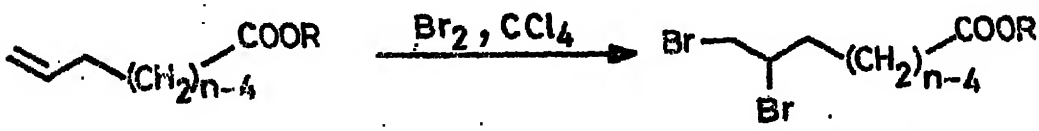
yield in the latter case should be considered representative since the crude bromide related to 22, was admixed with a very non-polar impurity (tlc).

The acetylenic acids, 22 and 33, were transformed to the methyl esters, 23 and 34, with MeOH-H_2SO_4 (catalyst) in quantitative yields, reduced with LAH to alcohols 24 (98%) and 35 (83%), which on protection with dihydropyran, using pyridinium paratoluene sulfonate (PPTS) as catalyst, gave the key synthons, 1-tetrahydropyranyloxy 10-undecyne (25) (96%) and 1-tetrahydropyranyloxy 9-decyne (36) (98%) (CHART I.C.5). PPTS[59] has been found to be an exceptionally good reagent, not only for the -OH $\longrightarrow$ -OTHP change but also for the reverse de-protection. The yields are superior and instead of the darkish reaction mixtures that usually result when PTSA is employed, the PPTS mediated changes proceed in clean, colourless media.

Prior to alkylation studies connected with insect sex-pheromone syntheses, the optimum conditions for acetylide formation was worked out by deuteration studies. In the present work, the best results were obtained using 2 moles of n-butyl lithium per mole of terminal acetylene. Thus 1-tetrahydropyranyloxy 10-undecyne was transformed, in quantitative yields to 11-deutero 1-tetrahydropyranyloxy 10-undecyne with, at least, 98% isotopic purity.

CHART I.C.5

Preparation of key synthons, 1-tetrahydropyranyloxy 10-undecyne (25) and 1-tetrahydropyranyloxy 9-decyne (36)

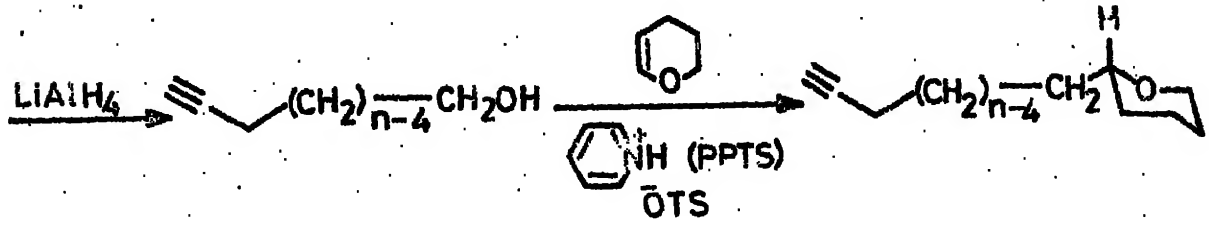


n = 11 ; R = Me ; 2
n = 10 ; R = H ; 10

n = 11 ; R = Me ; 21
n = 10 ; R = H ; 32

n = 11 ; 22
n = 10 ; 33

n = 11 ; 23
n = 10 ; 34



n = 11 ; 24
n = 10 ; 35

n = 11 ; 25
n = 10 ; 36

22: bp 124°/3 torr

ir : ν_{max}(neat)(cm^{-1}): 3310 (H-C≡C-), 2110 (-C≡C-), 1710 (acid).

nmr: $\delta_{(CCl_4)}$: 1.71 (t, 1H, -C≡C-H), 1.9-2.5 (m, 4H, $-CH_2-C\equiv C-H$, $-CH_2COOH$), 11.2 (s, 1H, -COOH).

33: bp 85-90°/0.05 torr

ir : ν_{max}(neat)(cm^{-1}): 3300 (H-C≡C), 2110 (C≡C), 1710 (acid).

nmr: $\delta_{(CCl_4)}$: 1.94 (t, 1H, H-C≡C-), 2.05-2.51 (m, 4H, $-C\equiv C-CH_2$, $-CH_2-COOH$), 11.3 (br, 1H, -COOH).

23: bp 77-80°/0.4 torr

ir : ν_{max}(neat)(cm^{-1}): 3310 (C-H), 2110 (-C≡C-), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 1.71 (t, 1H, -C≡C-H), 1.9-2.4 (m, 4H, $-CH_2-C\equiv C-$, $-CH_2-COOMe$), 3.54 (s, 3H, $-COOCH_3$).

34: bp 79-80°/0.05 torr

ir : ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2110 (-C≡C-), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 1.85 (t, 1H, H-C≡C-), 2.05-2.4 (m, 4H, $-C\equiv C-CH_2$, $-CH_2-COOCH_3$), 3.65 (s, 3H, $-COOCH_3$).

24: ir : ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl), 3310 (-C≡C-H), 2110 (-C≡C-).

nmr: $\delta_{(CCl_4)}$: 1.8 (t, 1H, -C≡C-H), 1.9-2.3 (m, 2H, $-CH_2-C\equiv C-$), 3.5 (t, 2H, $-CH_2-OH$), 3.6 (s, 1H, -OH).

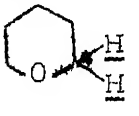
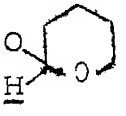
35: bp 74-75°/0.04 torr

ir : ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl), 3310 (-C≡C-H), 2110 (-C≡C-).

nmr: $\delta_{(CCl_4)}$: 1.81 (t, 1H, -C≡C-H), 1.95-2.3 (m, 2H, $-C\equiv C-CH_2-$), 3.55(t, 2H, $-CH_2-OH$), 3.6 (s, 1H, -OH).

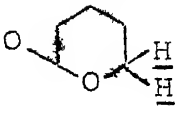
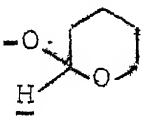
25: bp 88-90°/0.2 torr

ir : ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2110 (-C≡C-), 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 1.7 (t, 1H, -C≡C-H), 1.85-2.3 (m, 2H, $-CH_2-C\equiv C-$), 3.0-4.0 (m, 4H, $-CH_2-O$- ), 4.45 (s, 1H, -O- ).

36: bp 108-110°/0.05 torr

ir : ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2110 (-C≡C-), 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 1.85 (t, 1H, -C≡C-H), 2.0-2.5 (m, 2H, -C≡C-CH_2-), 3.0-4.0 (m, 4H, -CH_2-O- ), 4.5 (s, 1H, -O- ).

Synthesis of 1-acetoxy (Z) 10-pentadecene (31): Homolog of Spodoptera frugiperda pheromone

1-Tetrahydropyranyloxy 10-undecyne 25, the more easily available of the two acetylenic synthons, not only served as a good model for further transformations leading to the insect sex pheromones, but also was readily useful in the first synthesis of the pheromone related to Archips semiferanus.

In preliminary model studies, optimum conditions for acetylide alkylation was investigated with 25. Exchange studies with this compound had already shown the best conditions for acetylide formation (vide-supra). Of the various solvent systems investigated, HMPA was found to give best results in alkylation. Generally, alkylation of acetylides having hydrophobic segments, such as in the present work, is not very easy. In the event, 25 was transformed, via alkylation of the lithium acetylide with 2 equivalents of n-BuBr in HMPA at 25° to 1-tetrahydropyranyloxy 10-pentadecyne (29) (96%). The latter was directly transformed to 1-acetoxy 10-pentadecyne (30) in

88% yields, with AcOH:AcCl::10:1. Stereoselective hydrogenation of 30 using 5% $Pd/BaSO_4$, further deactivated with a very small amount of synthetic quinoline, gave 1-acetoxy (Z) 10-pentadecene (31) (99%) (CHART I.C.6).

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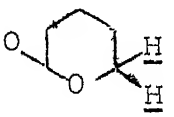
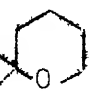
29 : bp 125-7°/0.02 torr

ir : ν_{max}(neat) (cm^{-1}): 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 0.85 (t, 3H, $-CH_3$), 1.85-2.2 (m, 4H, $-CH_2-C\equiv C-CH_2-$), 3.0-4.0 (m, 4H, $-CH_2-O$ ), 4.4 (s, 1H, $-O$ ).

30: bp 81-82°/0.02 torr

ir : ν_{max}(neat) (cm^{-1}): 1735 (acetate).

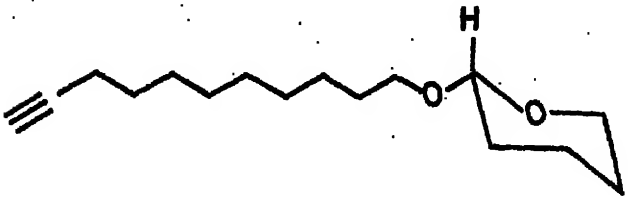
nmr: $\delta_{(CCl_4)}$: 0.85 (t, 3H, $-CH_3$), 1.85-2.2 (m, 7H, $-OCOCH_3$, $-CH_2-C\equiv C-CH_2-$), 3.9 (t, 2H, $-CH_2-OCOCH_3$).

31: ir : ν_{max}(neat) (cm^{-1}): 1735 (acetate).

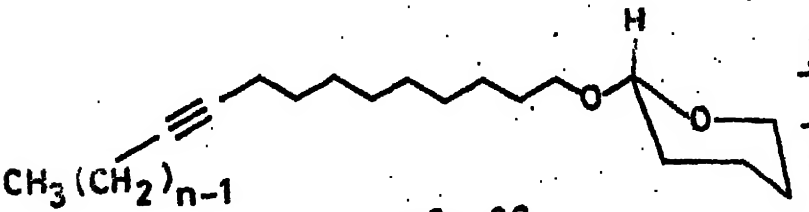
nmr: $\delta_{(CCl_4)}$: 0.85 (t, 3H, $-CH_3$), 1.85-2.2 (m, 7H, $-OCOCH_3$, $-CH_2-C=C-CH_2-$), 3.9 (t, 2H, $-CH_2-OCOCH_3$), 5.08-5.35 (m, 2H, olefinic).

CHART I.C.6

Synthesis of pheromone of Archips semiferanus (28) and the homolog of Spodoptera frugiperda pheromone (31)



1. n-BuLi, HMPA
2. $CH_3-(CH_2)_{n-1}-Br$

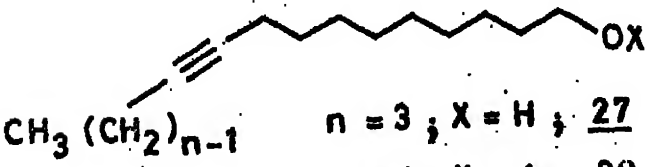


26: PPTS–EtOH

29: AcOH/AcCl

n = 3 ; 26

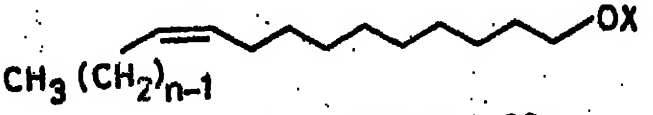
n = 4 ; 29



n = 3 ; X = H ; 27

n = 4 ; X = Ac ; 30

$Pd/BaSO_4$
Quinoline
H_2



n = 3 ; X = H ; 28

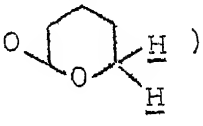
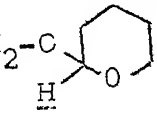
n = 4 ; X = Ac ; 31

Synthesis of (Z) 10-tetradecenol (28): The sex pheromone of Archips semiferanus

The ready availability of synthon, 1-tetrahydropyranyloxy 10-undecyne (25), from castor oil, made it possible to achieve the first synthesis of pheromone related to Archips semiferanus. Thus, the alkylation of lithium acetylide related to 25 with n-PrBr in HMPA gave 1-tetrahydropyranyloxy 10-tetradecyne (26) (94%) which was deprotected with PPTS-EtOH to alcohol 27 (92%) and then by stereoselective hydrogenation over Pd-$BaSO_4$ converted to the pheromone 28 (97%). In every way, the present synthesis should be the most facile route to 28 (CHART I.C.6).

26: bp 118-120°/0.05 torr

ir : ν_{max}(neat)(cm^{-1}): 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-CH_3$), 1.85-2.2 (m, 4H, $-CH_2-C\equiv C-CH_2-$), 3.0-4.0 (m, 4H, $-CH_2-O$ ), 4.4 (s, 1H, CH_2-C ).

27: bp 90-95°/0.05 torr

ir : ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-CH_3$), 1.85-2.2 (m, 4H, $-CH_2-C\equiv C-CH_2$), 3.4 (t, 2H, $-CH_2-OH$), 3.72(s,1H, $-OH$).

28: ir : ν_{max}(neat) (cm^{-1}): 3330 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.85 (t, 3H, $-C\underline{H}_3$), 1.75-2.15 (m, 4H, $-C\underline{H}_2-C=C-C\underline{H}_2-$), 3.5(t, 2H, $-C\underline{H}_2OH$), 3.6 (s, 1H, $-O\underline{H}$), 5.05-5.35 (m, 2H, $-C\underline{H}=C\underline{H}-$).

Synthesis of 1-acetoxy (Z) 9-tetradecene (39): The pheromone of Spodoptera frugiperda

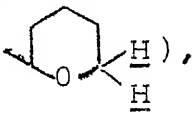
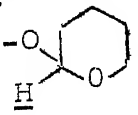
135,000 Abdominal tips of virgin females of the species Spodoptera frugiperda on extraction and purification gave five components, of which only one, namely, 1-acetoxy (Z) 9-tetradecene (39) was attractive to males. The yield was 0.0009 g. The S. frugiperda is an apple pest and endeavours have been made to use the pheromone to lure the insects to a restricted area so that insecticides can be selectively applied.

In the present work, the synthesis of the pheromone of S. frugiperda was achieved from 1-tetrahydropyranyloxy 9-decyne (36). The lithium acetylide from 36 was alkylated with n-BuBr in HMPA to give 1-tetrahydropyranyloxy 9-tetradecyne (37) (96%) which was directly transformed with AcOH:AcCl::10:1 to 1-acetoxy 9-tetradecyne (38) (89%). The latter on stereoselective hydrogenation over Pd-$BaSO_4$ gave 1-acetoxy (Z) 9-tetradecene (39) (99%) (CHART I.C.7). GC analysis of this sample by Dr. Hall

on 6'x2 mm i.d. 5% SE 30/0.5% carbowax 20 M/chromosorb W HP, 6'x2 mm i.d. 1.5% carbowax 20 M/chromosorb G Aw DMCS and 1.8 m x 2 mm i.d. 5% 4-(p-methoxycinnamyloxy)-4'-methoxyazobenzene columns, showed that it contained 5.57% unalkylated material and that the sample was, at least, 95% the desired Z isomer. Dr. Hall has further suggested that the stereochemical purity can be increased to ∿ 98% by hydrogenation at lower temperatures. The present route to the Spodoptera frugiperda sex pheromone is attractive in comparison to the other procedures, since it would be difficult to delineate a pathway easier than that described in the present work, with reference to availability of starting material, yields and stereochemical purity.

37: bp 128-130°/0.03 torr

ir : ν_{max}(neat) (cm^{-1}): 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $-CH_3$), 2.0-2.25 (m, 4H, $-CH_2-C\equiv C-CH_2-$), 3.0-4.0 (m, 4H, $-CH_2-O$ ), 4.5 (s, 1H, ).

38: bp 70-75°/0.05 torr

ir : ν_{max}(neat) (cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $-CH_3$), 1.98 (s, 3H, $-OCOCH_3$), 2.0-2.25(m, 4H, $-CH_2-C\equiv C-CH_2-$), 3.95 (t, 2H, $-CH_2-OAc$).

39: bp 110-115°/0.05 torr

ir : ν_{max}(neat)(cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-C\underline{H}_3$), 1.8-2.25 (br, 7H, $-OCOC\underline{H}_3$, $-C\underline{H}_2-C=C-C\underline{H}_2-$), 3.95 (t, 2H, $-C\underline{H}_2-OAc$), 5.32 (m, 2H, olefinic).

Synthesis of 1-acetoxy (Z) 9-dodecene (42): The pheromone of Paralobesia viteana (Grape berry moth)

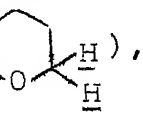
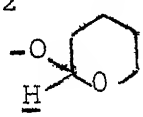
This potent pheromone present in virgin females of the species P. viteana can lure males in the field within a zone of, at least, 40 kilometres. The number of males lured is related to the age of the females and the weather ! Sex pheromone traps baited with "grapemone" (91% pure 1-acetoxy (Z) 9-dodedecene) and set out in vineyards attracted, not only the grape berry moth, which does cause economic damage, but also E. argutanus, which is apparently economically innocuous. These experiments have demonstrated that a Z:E.:95:5 ratio constitutes the best combination.

1-Tetrahydropyranyloxy 9-decyne (36) was alkylated, via the lithium salt, with EtBr in HMPA to 1-tetrahydropyranyloxy 9-dodecyne (40) (98%). Compound 40 was directly transformed with AcOH:AcCl::10:1 to 1-acetoxy 9-dodecyne (41) (94%), which on

stereoselective hydrogenation over Pd-$BaSO_4$ gave, in 99% yields, the pheromone 1-acetoxy (Z) 9-dodecene (42) (CHART I.C.7). The stereochemical purity of 42 is inferred to be around 95% based on an analysis of the related 1-acetoxy (Z) 11-tetradecene.[60] The procedure described in the present work is amongst the best that are available amongst the many (SECTION I.B.) for this important pheromone.

40: bp 92-93°/0.05 torr

ir : ν_{max}(neat) (cm^{-1}): 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 1.1 (t, 3H, $-C\underline{H}_3$), 1.95-2.25 (m, 4H, $-CH_2-C\equiv C-C\underline{H}_2-$), 3.0-4.0 (m, 4H, $-C\underline{H}_2-O-$ ), 4.5 (s, 1H, ).

41: bp 75-80°/0.05 torr

ir : ν_{max}(neat) (cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 1.1 (t, 3H, $-C\underline{H}_3$), 1.95 (s, 3H, $-OCOC\underline{H}_3$), 2.0-2.25 (m, 4H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 4.0 (t, 2H, $-C\underline{H}_2-OAc$).

42: ir : ν_{max}(neat) (cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $-C\underline{H}_3$), 1.9-2.25 (m, 7H, $-OCOC\underline{H}_3$, $-C\underline{H}_2-C=C-C\underline{H}_2-$), 3.95 (t, 2H, $-C\underline{H}_2-OAc$), 5.3 (m, 2H, olefinic).

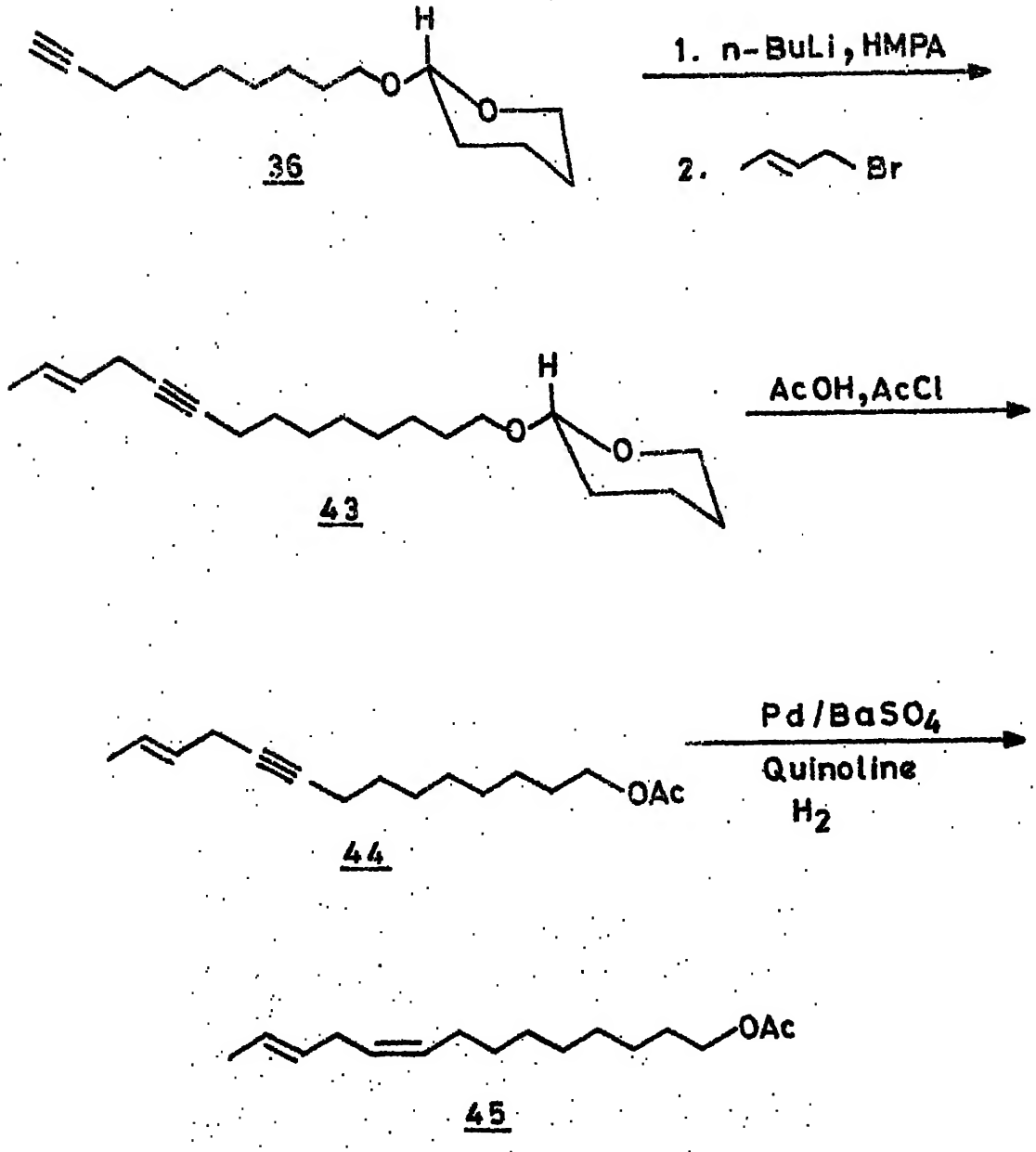
Synthesis of 1-acetoxy (Z)(E) 9,12-tetradecadiene (45): The pheromone of Prodenia eridania (Prodenialure)

An extract of 309,000 virgin female abdomens of the species, P. eridania gave 0.004 g of 1-acetoxy (Z) 9-tetradecene (Prodenialure A, 39) and 0.0008 g of 1-acetoxy (Z)(E) 9,12-tetradecadiene (Prodenialure B, 45). In field trials a combination of A and B was needed to attract male moths into traps.

The synthesis of Prodenialure B was accomplished, in the present work, from 1-tetrahydropyranyloxy 9-decyne 36, by alkylation of the lithium salt with crotyl bromide to yield the ene yne 43 (98%) which was directly transformed with AcOH:AcCl::10:1 to 1-acetoxy tetradec 12-ene 9-yne (44) (99%) and then stereoselectively hydrogenated over Pd-$BaSO_4$ to 45 (98%) (CHART I.C.8). Surprisingly, a GC analyses of this sample by Dr. Hall showed that it was a mixture wherein the expected Z,E isomer was, at best, present to the extent of 40% only. It is surmised that the mixture resulted from isomerisation of the originally pure preparation, since the procedure warranted the expected Z,E isomer. Such isomerisation could have resulted either during transit or during attempted purification by preparative tlc. Prodenialure, being possessed of a skipped π system, appears to be quite sensitive to isomerisation. With proper precautions the present procedure must lead to a more stereochemically pure sample.

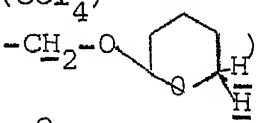
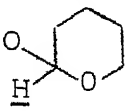
CHART I.C.8

Synthesis of Prodeniafure (45)



43: bp 105°/0.05 torr

ir : ν_{max}(neat) (cm^{-1}): 1135(s), 1120(s), 1030(s), 980(m), 900(m), 870(m), 815(m), 970 (trans double bond).

nmr: $\delta_{(CCl_4)}$: 2.1(br, -CH=CH-CH_2-C≡C-), 3.1-4.0(m, 4H, ), 4.6(s, 1H, ) 5.4-5.7(m, olefinic).

44: bp 105-107°/0.05 torr

ir : ν_{max}(neat) (cm^{-1}): 1735 (acetate), 970 (trans double bond).

nmr: $\delta_{(CCl_4)}$: 1.75 (t, 3H, $-CH_3$), 1.95-2.2 (m, 5H, $-OCOCH_3$, -HC=CH-CH_2-C≡C-), 4.01 (t, 2H, $-CH_2$-OAc), 5.3-5.95 (m, 2H, olefinic).

45: ir : ν_{max}(neat) (cm^{-1}): 1735 (acetate), 970 (trans double bond).

nmr: $\delta_{(CCl_4)}$: 1.6 (t, 3H, $-CH_3$), 1.9 (s, 3H, $-OCOCH_3$), 2.5-2.8 (m, 2H, -HC=CH-CH_2-CH=CH-), 3.9 (t, 2H, $-CH_2$-OAc), 4.95-5.6 (br, 4H, olefinic).

Synthesis of (Z) 9-tetradecenal (48): The pheromone of tobacco bud worm (Heliothis virescens)

Tobacco bud worm is an economic pest. From a large number of the H. virescens females, (Z) 9-tetradecenal (48), and

(Z) 11-hexadecenal were isolated in the ratio of 1:16. The synthetic 1:16 mixture elicited intense male response in the laboratory, although, individually they were found to be inactive. In field tests, as little as 0.000053 g of this mixture effectively competed with as many as 4 virgin females in luring males !

The synthesis of the tobacco bud worm was achieved, in the present work, by an exceptionally simple route by the de-protection of 1-tetrahydropyranyloxy 9-tetradecyne (37), by PPTS-EtOH, to 1-hydroxy 9-tetradecyne (46) (92%) followed by stereoselective hydrogenation over Pd-$BaSO_4$ to 1-hydroxy (Z) 9-tetradecene (47) (98%) and PCC oxidation in 89% yields (CHART I.C.9). The stereochemical purity of the pheromone 48 thus prepared is inferred to be, at least, 95% based on GC analysis of the related 39 (vide supra).

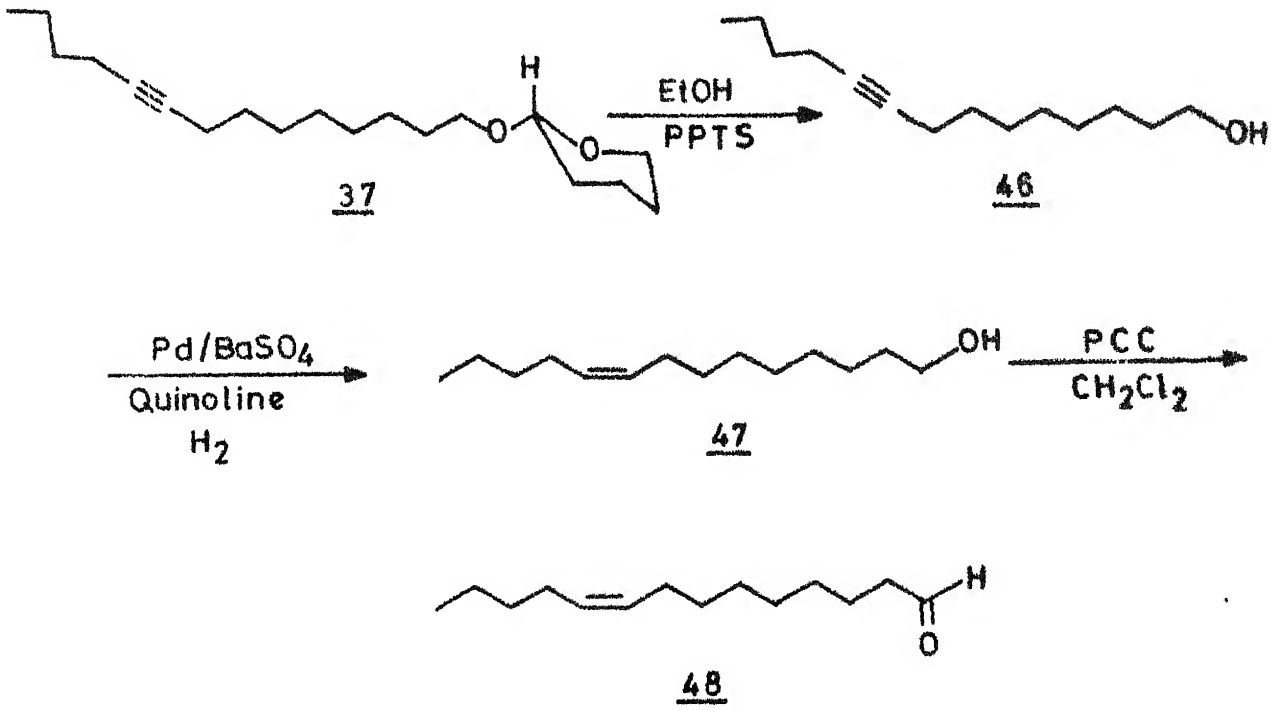
46: bp $100^{\circ}/0.05$ torr

ir : ν_{max}(neat)(cm^{-1}): 3325 (hydroxy).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-CH_3$), 1.95-2.35 (br, 4H, $H_2C-C\equiv C-CH_2-$), 2.85 (s, 1H, -OH), 3.45 (t, 2H, $-CH_2OH$).

CHART I.C.9

Synthesis of pheromone of Heliothis virescens (48)



47: bp 85-87°/0.03 torr

ir : ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-CH_3$), 1.8-2.25 (m, 4H, $-CH_2C{=}C-CH_2-$), 3.5(t, 2H, $-CH_2OH$), 3.7(s, 1H, $-OH$), 5.1-5.4 (m, 2H, olefinic).

48: ir : ν_{max}(neat)(cm^{-1}): 1730 (aldehyde).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $-CH_3$), 1.85-2.2 (m, 4H, $-CH_2-C{=}C-CH_2-$), 2.34 (t, 2H, $-CH_2-CHO$), 5.2-5.5 (m, 2H, olefinic), 9.7 (s, 1H, $-CHO$).

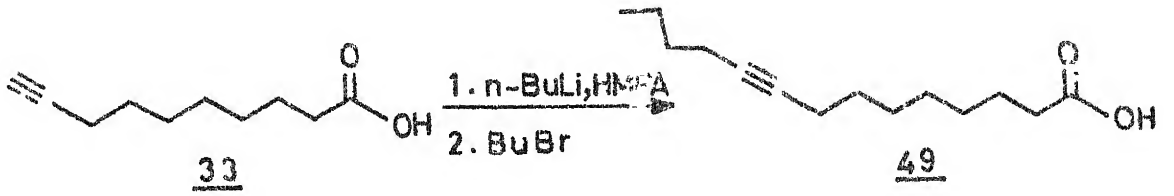
Synthesis of ethyl (Z) 9-tetradecenoate (51): The pheromone of Bombus lucorum

The synthesis of 51 involved the crucial alkylation of the acetylenic acid 33. This was accomplished by selective C-alkylation of the dilithium salt of 33 with n-BuBr in HMPA leading to 9-tetradecynoic acid (49) (100%). The latter was converted to the ethyl ester 50 (78%) and stereoselectively hydrogenated over Pd-$BaSO_4$ to the pheromone 51 (98%) (CHART I.C.10).

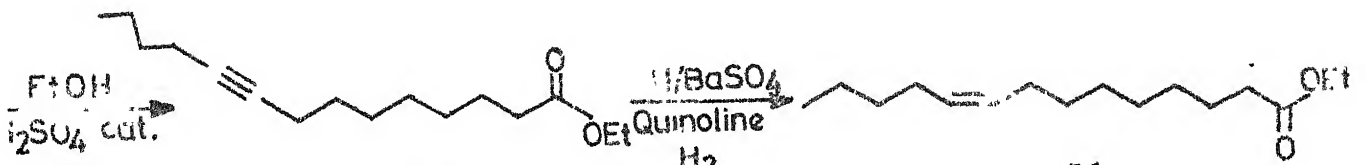
49: ir : ν_{max}(neat)(cm^{-1}): 1700 (acid).

CHART I.C.10

Synthesis of pheromone of Bombus lucorum (51)



33 49



50 51

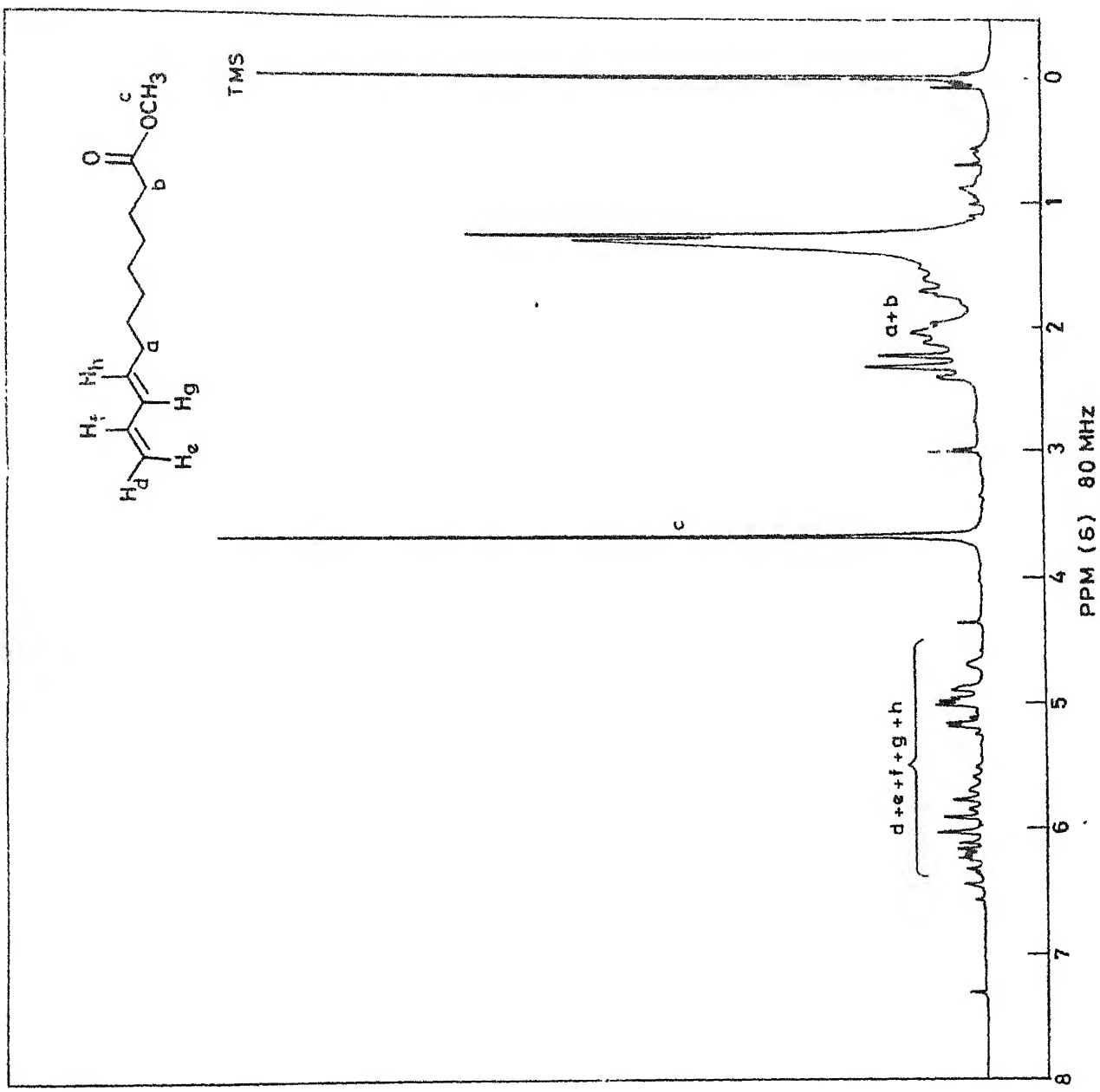
50: bp 94-95°/0.05 torr

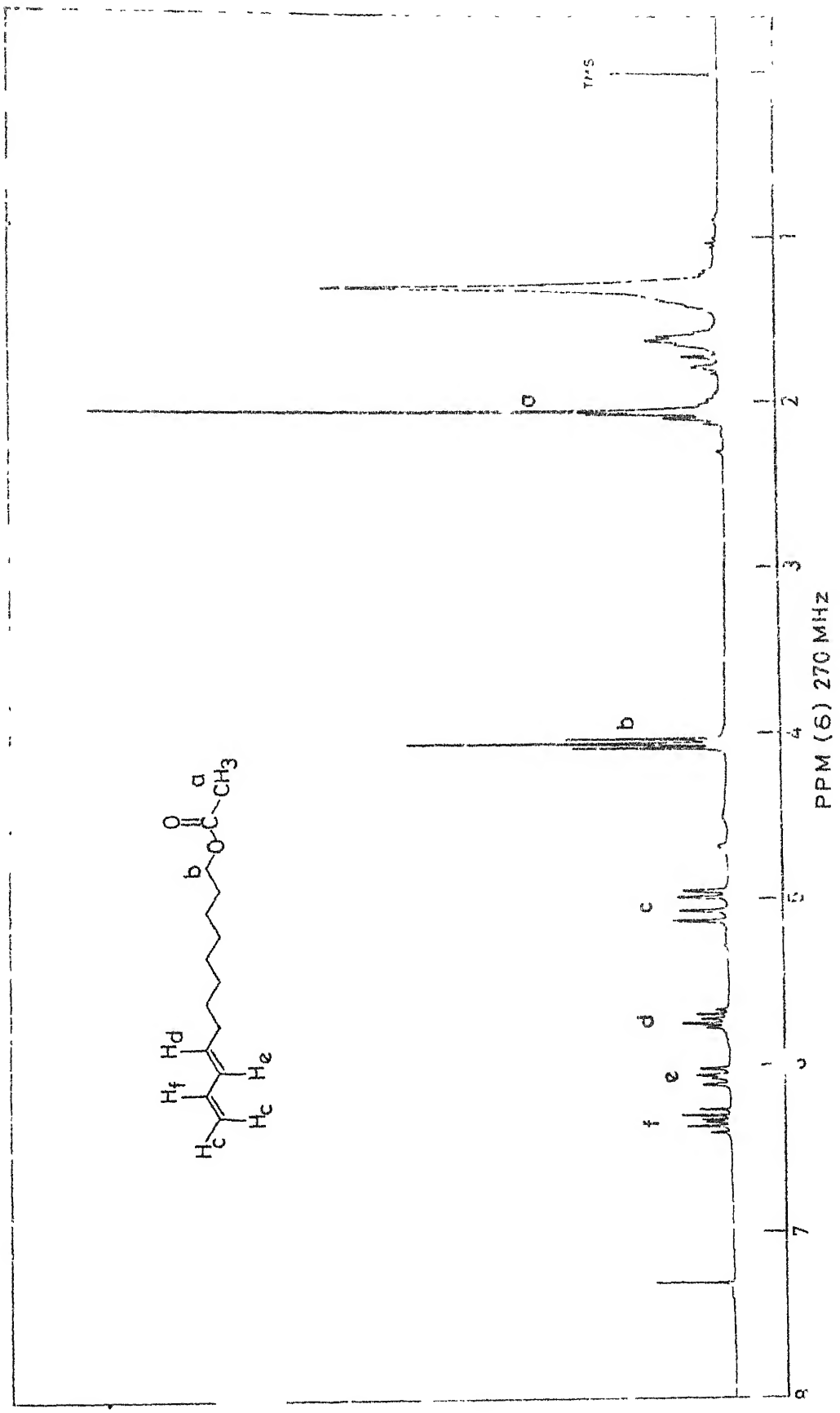
ir : ν_{max}(neat)(cm^{-1}): 1740 (ester).

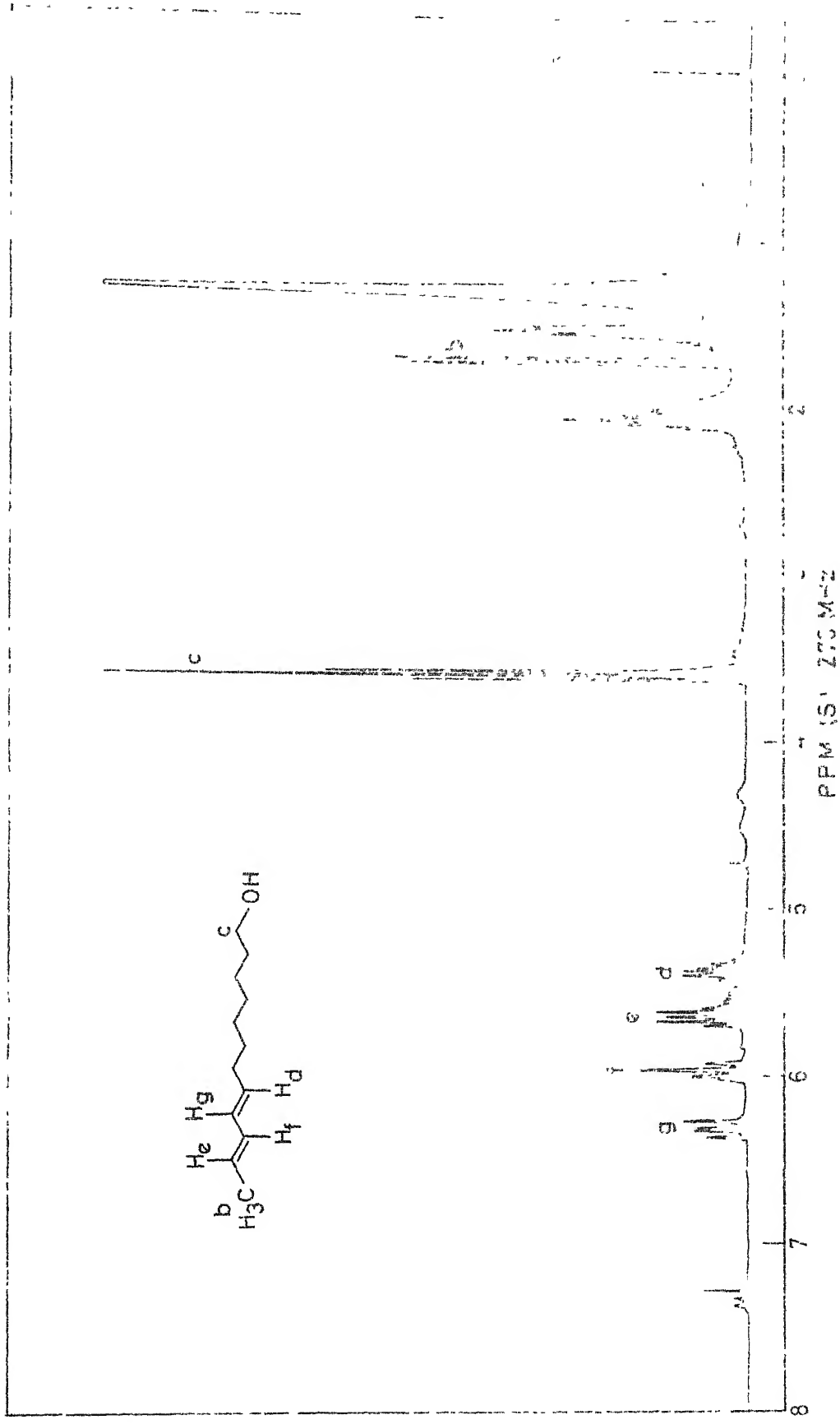
nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-C\underline{H}_3$), 1.2 (t, 3H, $-OCOCH_2C\underline{H}_3$), 2.0-2.4 (m, 6H, $-C\underline{H}_2COOC_2H_5$, $-C\underline{H}_2-C\equiv C-C\underline{H}_2$), 4.05 (q, 2H, $-OCOC\underline{H}_2CH_3$).

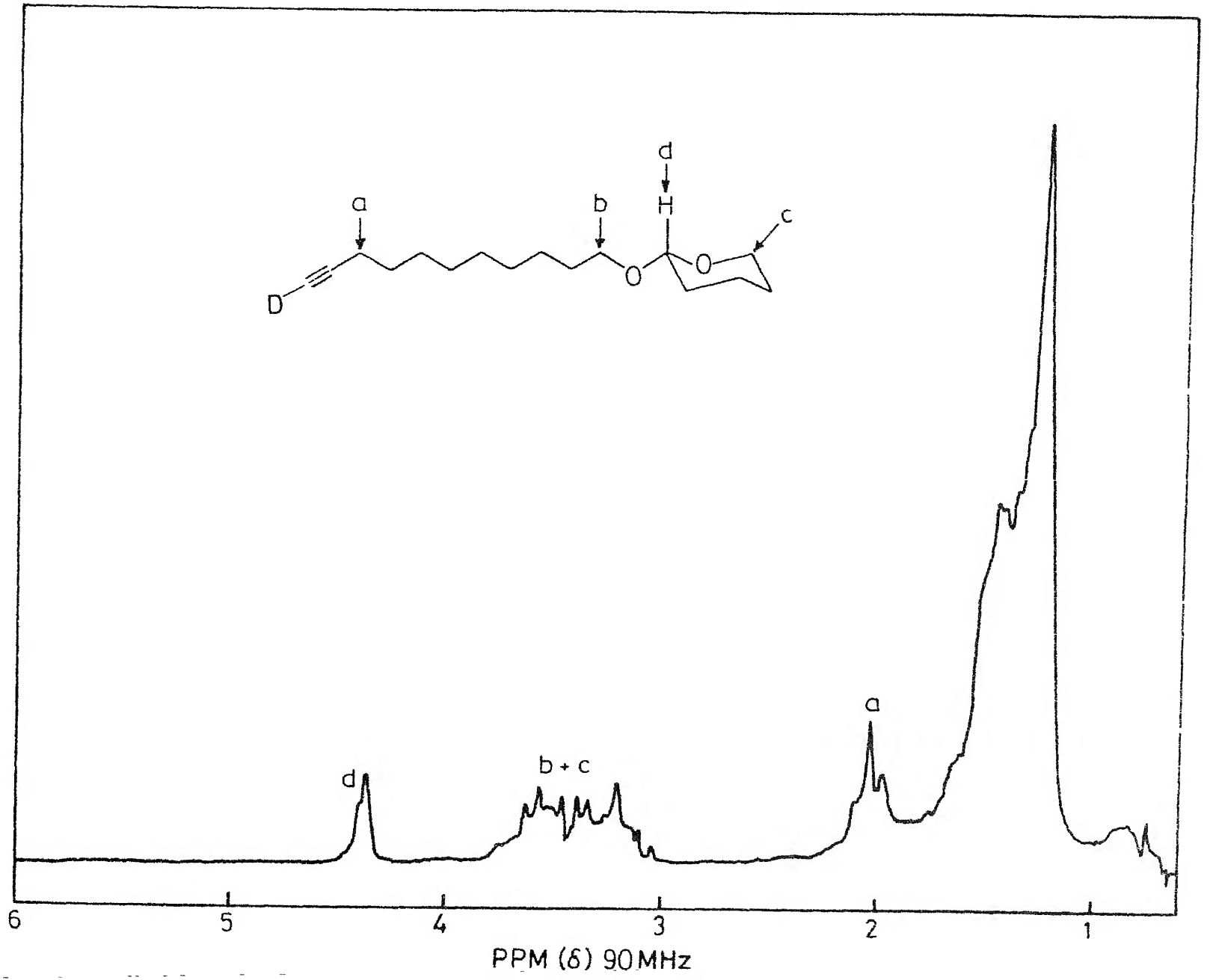
51: ir : ν_{max}(neat)(cm^{-1}): 1740 (ester).

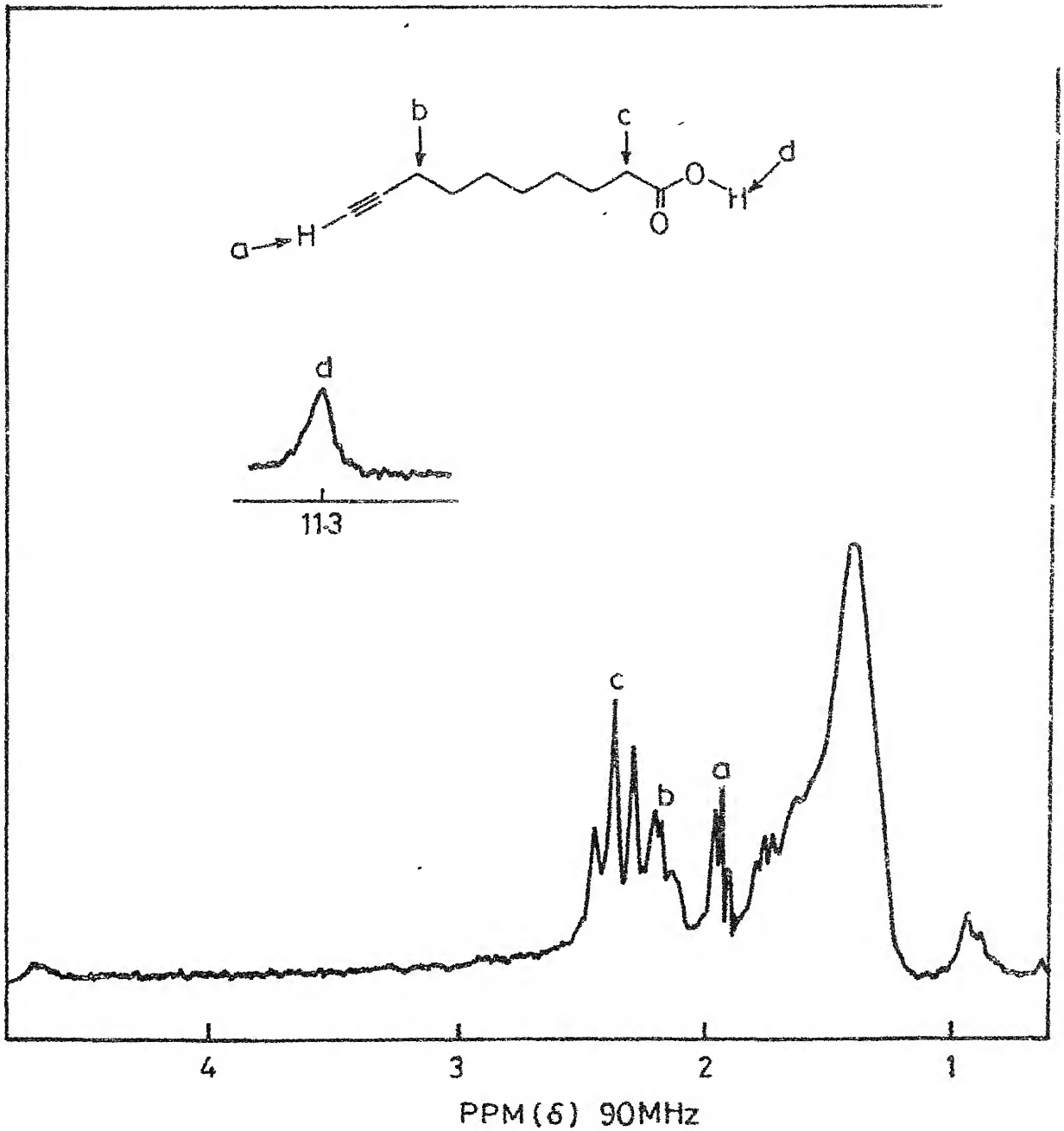
nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-C\underline{H}_3$), 1.21 (t, 3H, $-COOCH_2C\underline{H}_3$), 1.85-2.35 (m, 6H, $-C\underline{H}_2COOC_2H_5$, $-C\underline{H}_2-C=C-C\underline{H}_2-$), 4.05 (q, 2H, $-COOC\underline{H}_2CH_3$), 5.2-5.45 (m, 2H, olefinic).

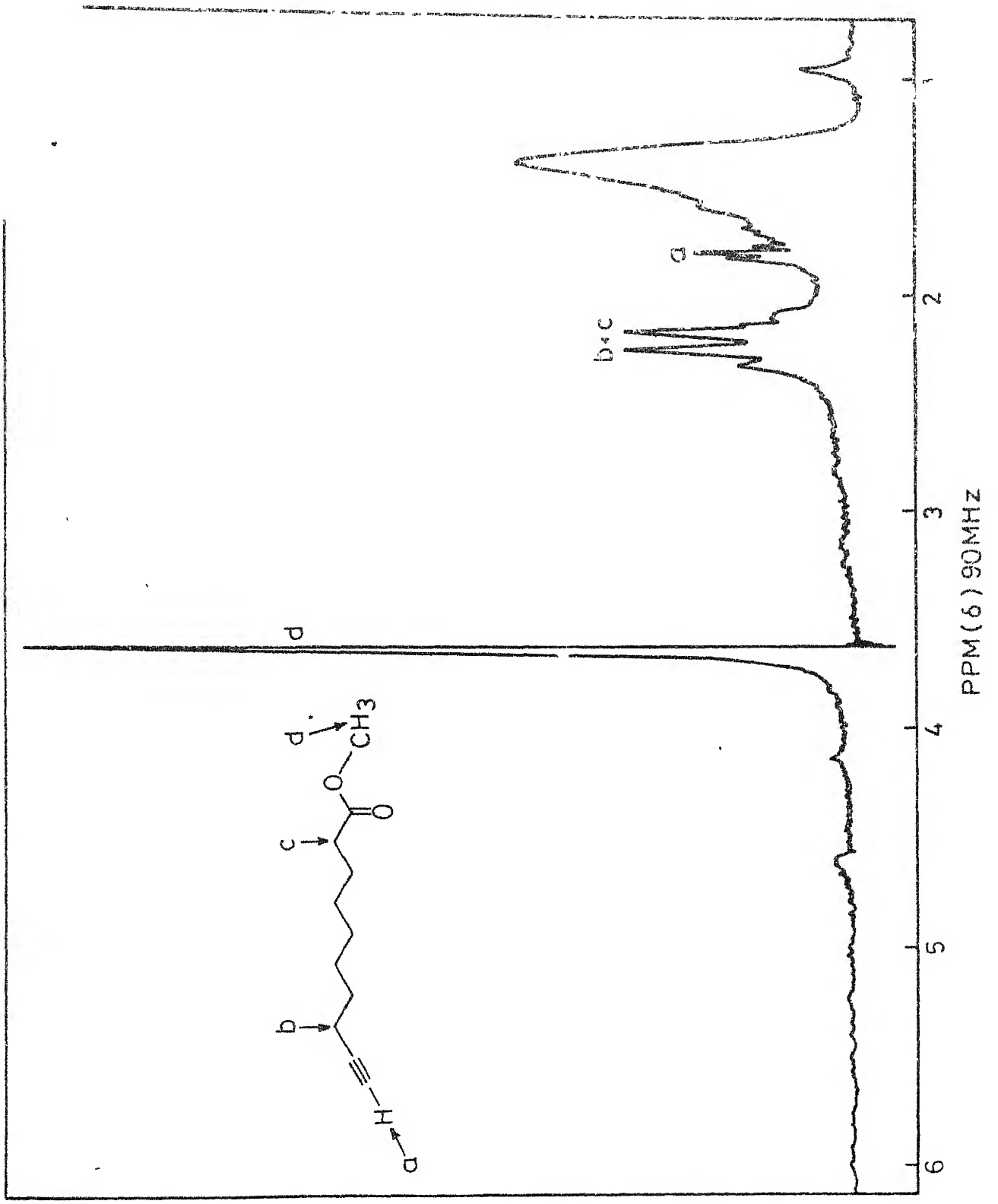

TMS
c
a+b
d+e+f+g+h
PPM (δ) 80 MHz
0
1
2
3
4
5
6
7
8
O
OCH3
a
b
c
Hd
He
Hf
Hg
Hh

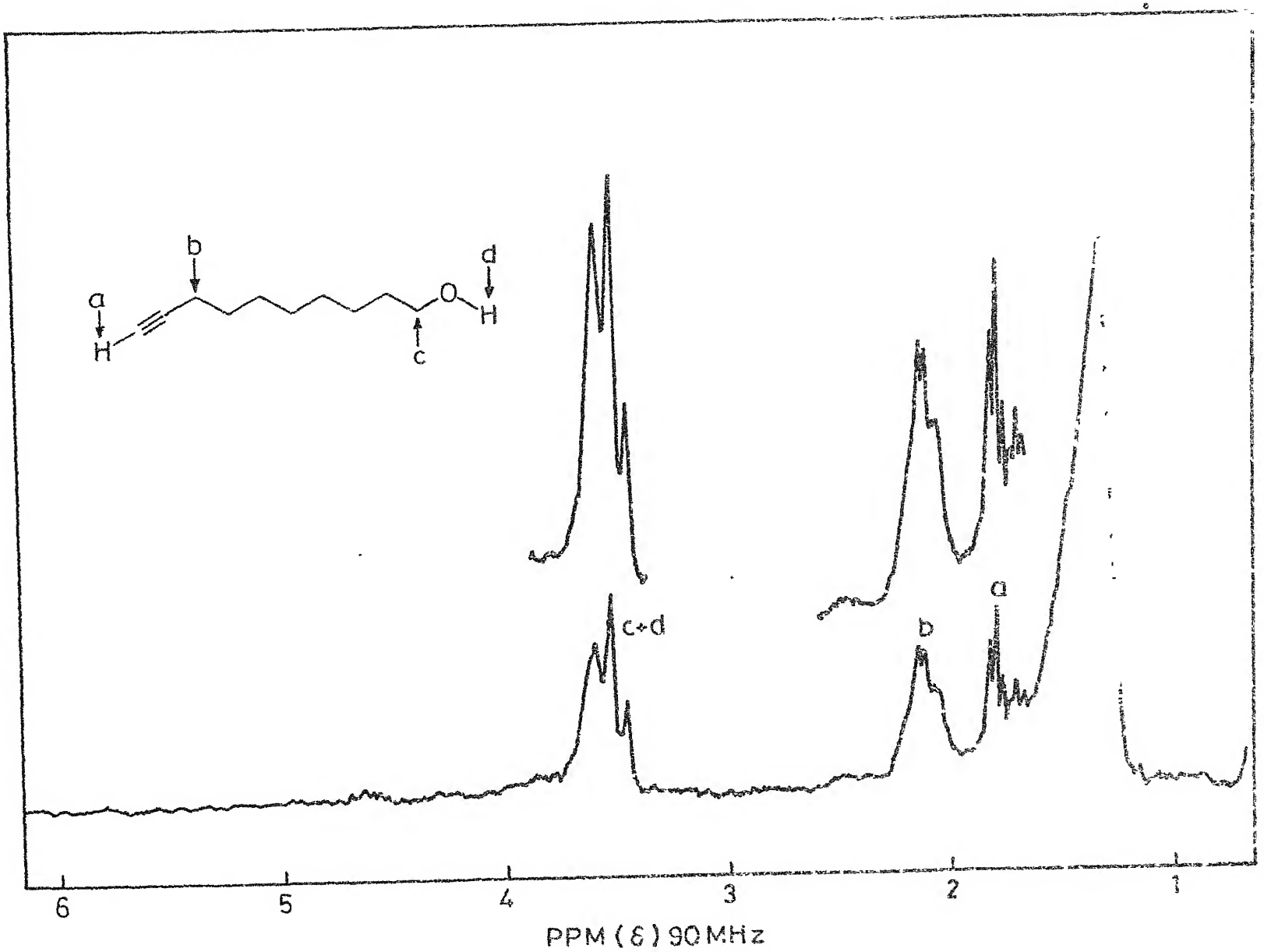

TMS
a
b
c
d
e
f
PPM (δ) 270 MHz
O
C
O
CH3
Hd
Hf
He
Hc
H3C

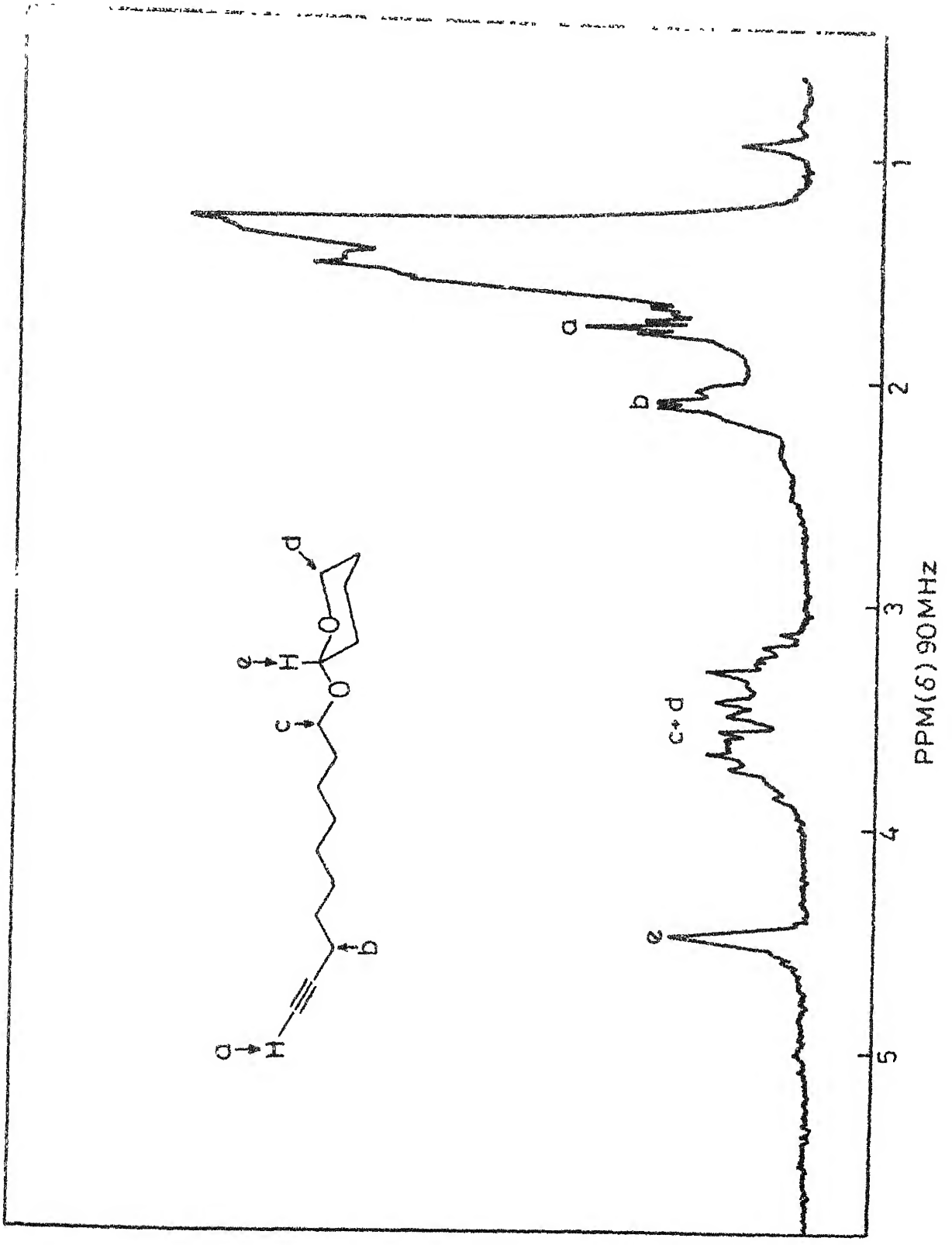

PPM (S') 270 MHz
OH
c
b
H_3C
H_e
H_g
H_f
H_d
a
e
d
c
b
a
1
2
3
4
5
6
7
8

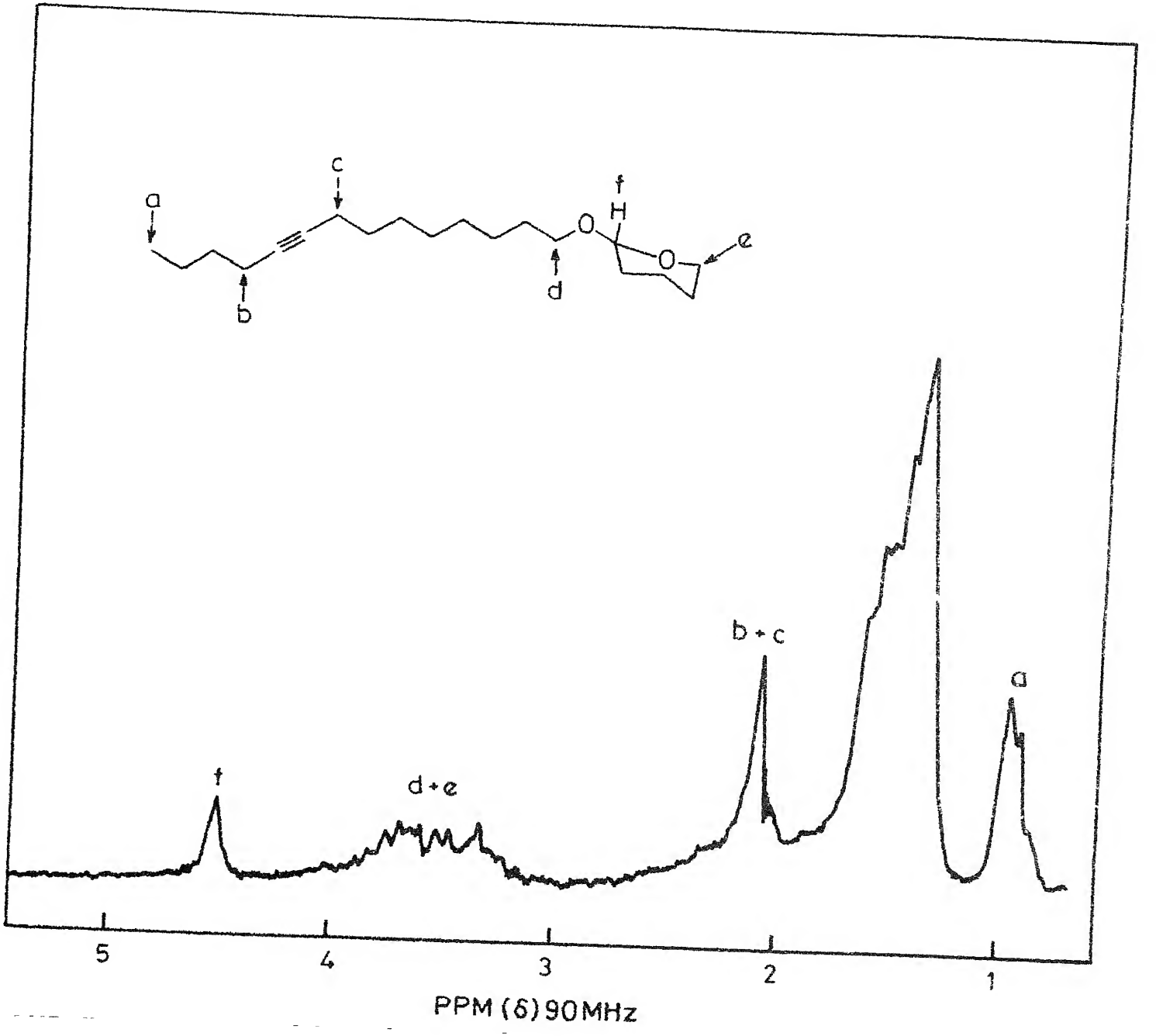

a
b
d
H
c
D
O
O
d
b + c
a
6
5
4
3
2
1
PPM (δ) 90 MHz

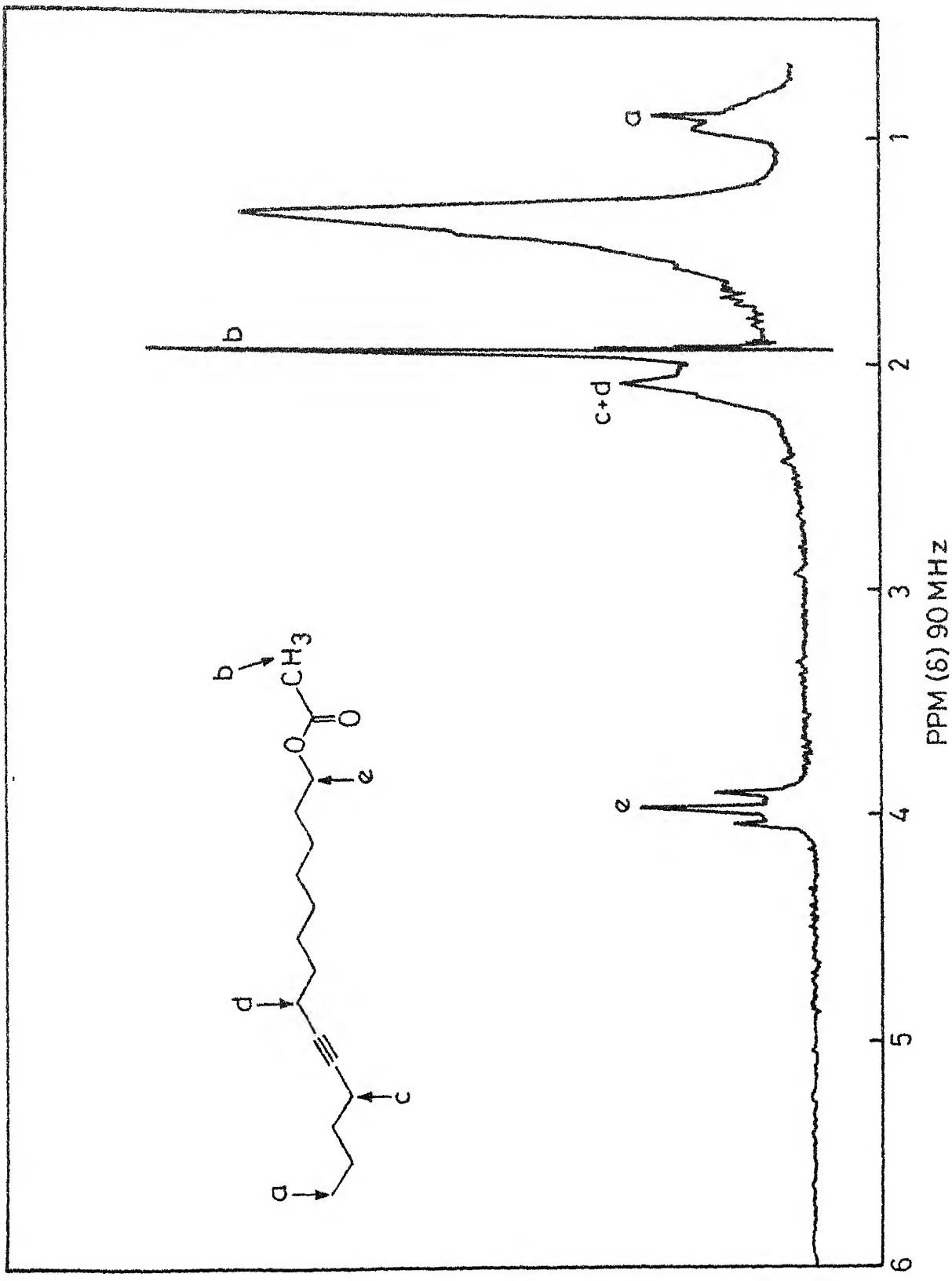

b
c
d
a
H
O
O
H
d
11·3
c
b
a
4
3
2
1
PPM (δ) 90MHz

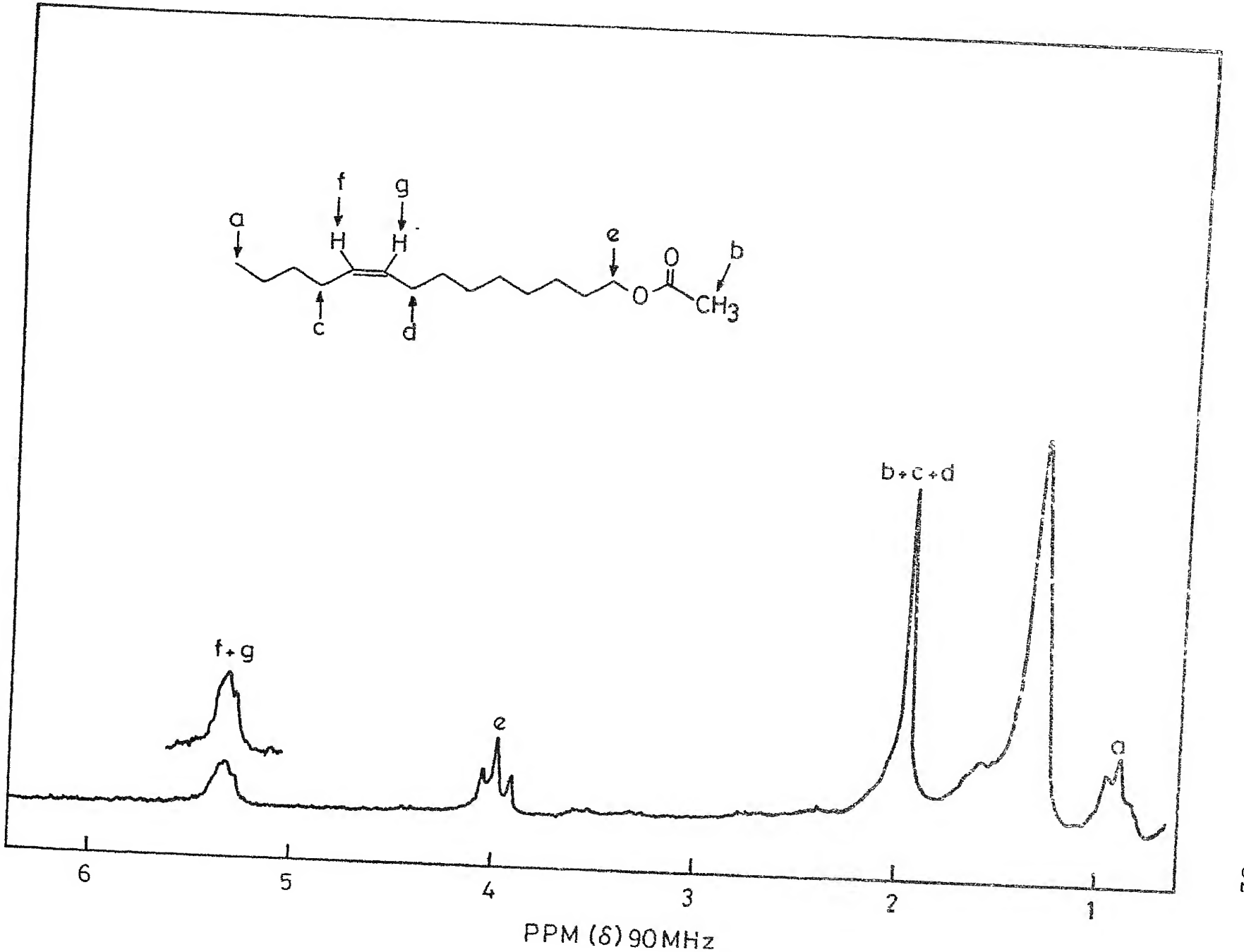

d
a
b+c
d
c
b
a
O
O
CH3
H
1
2
3
4
5
6
PPM(δ) 90MHz

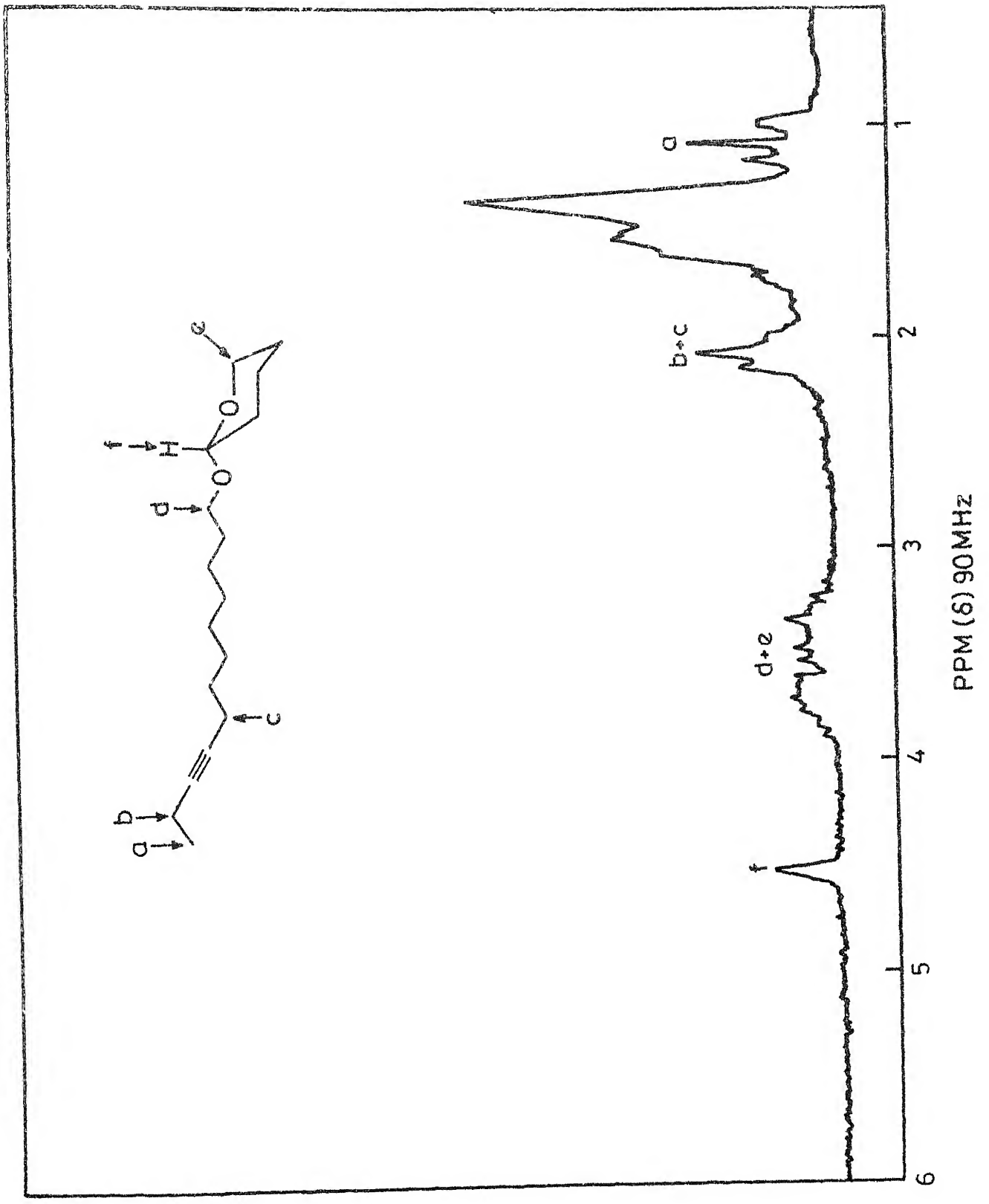

a
H
b
c
O
d
H
c+d
b
a
6
5
4
3
2
1
PPM (δ) 90 MHz

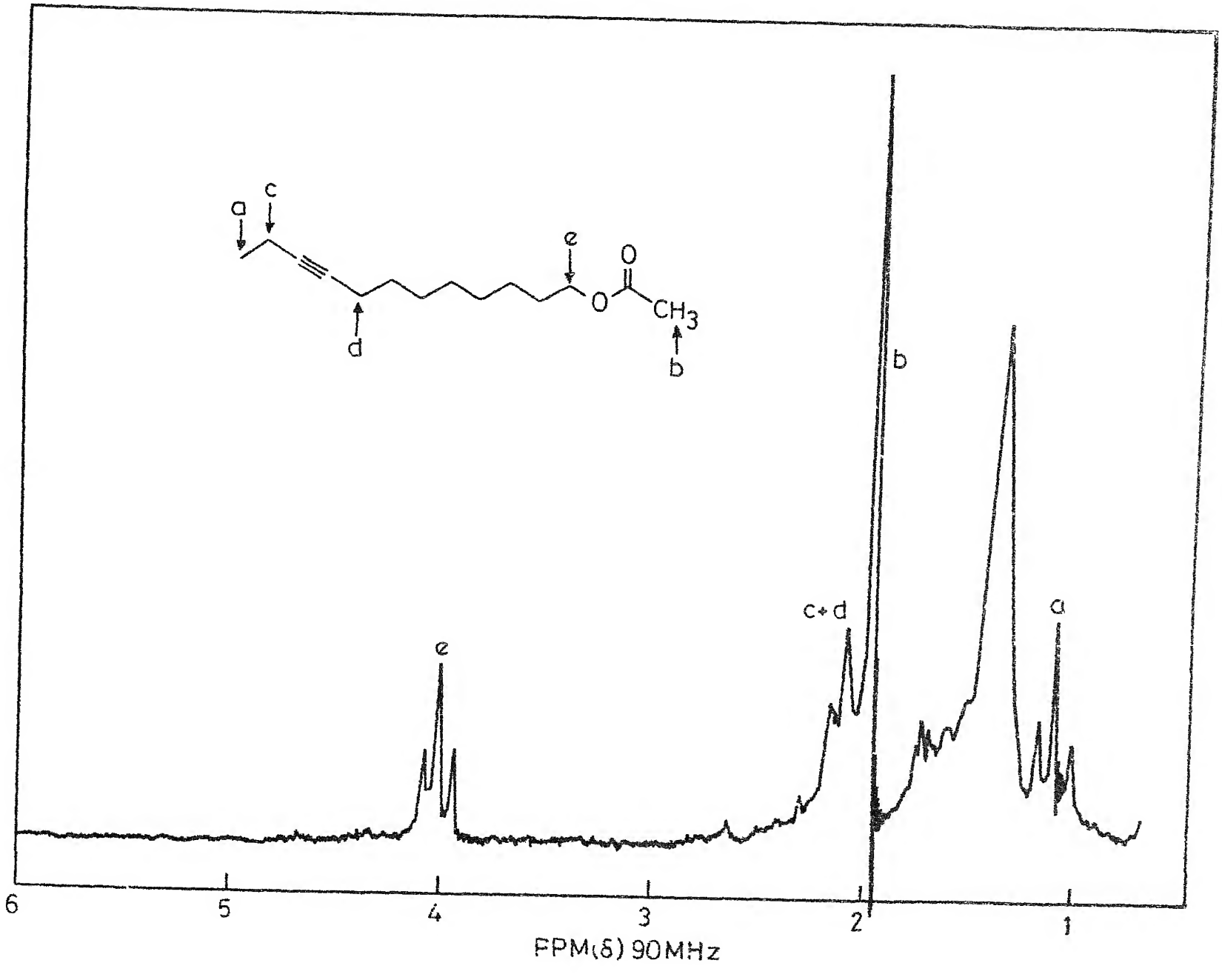

a
b
c+d
e
1
2
3
4
5
PPM(δ) 90MHz
a
b
c
d
e
H
O
O
H

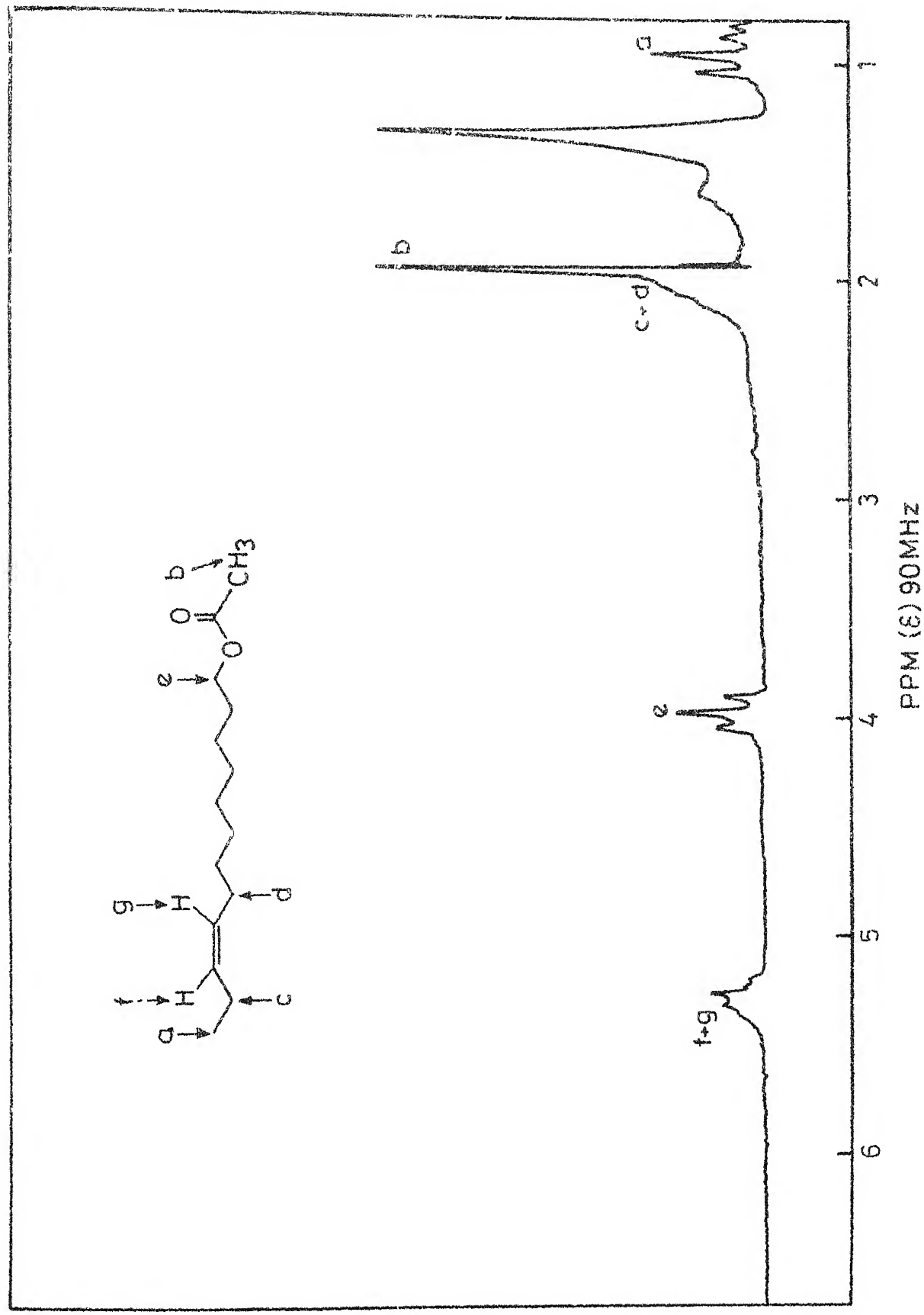

a
b
c
d
e
f
H
O
O
f
d+e
b+c
a
5
4
3
2
1
PPM (δ) 90 MHz

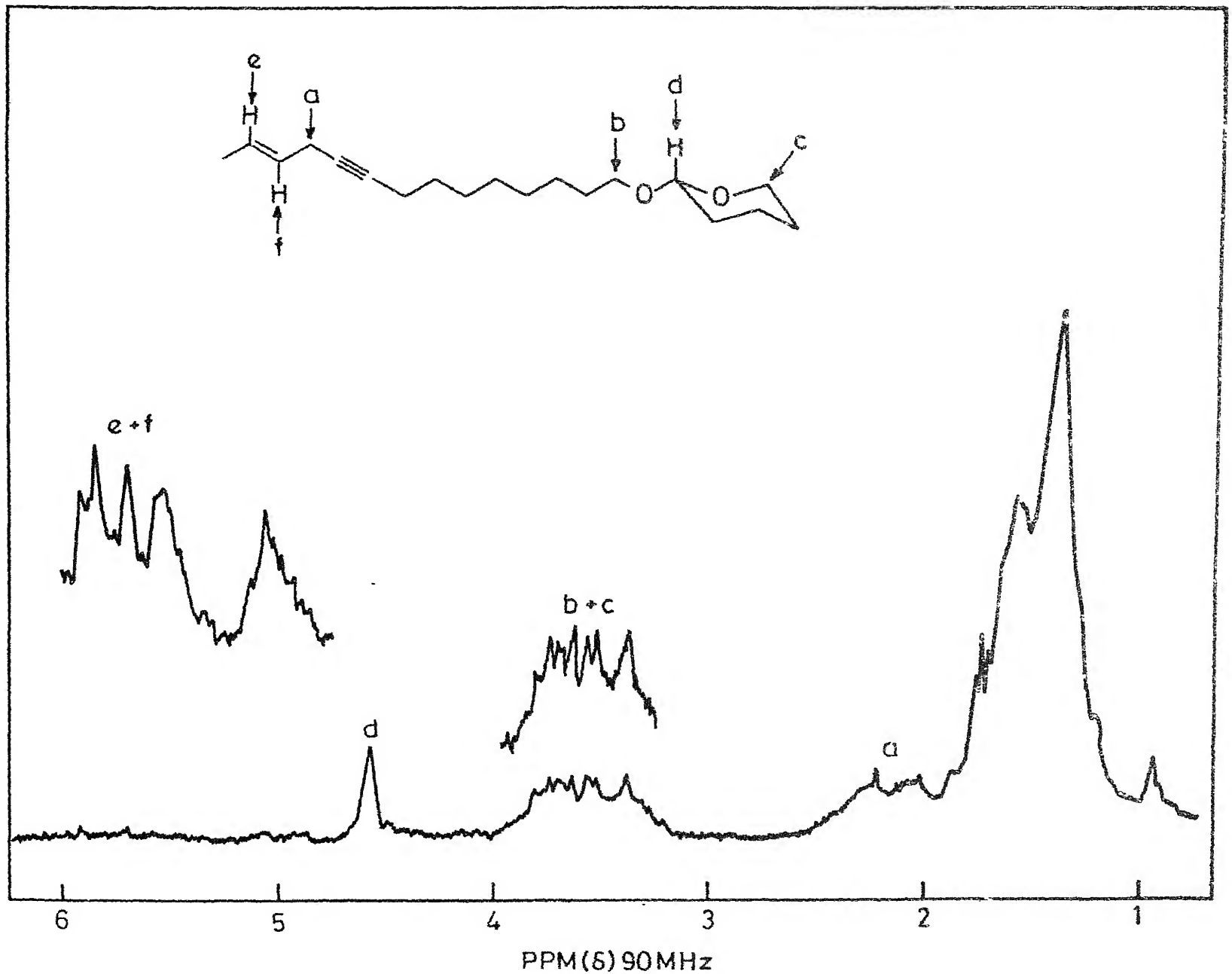

a
b
c
d
e
CH_3
O
O
a
b
c+d
e
1
2
3
4
5
6
PPM (δ) 90 MHz

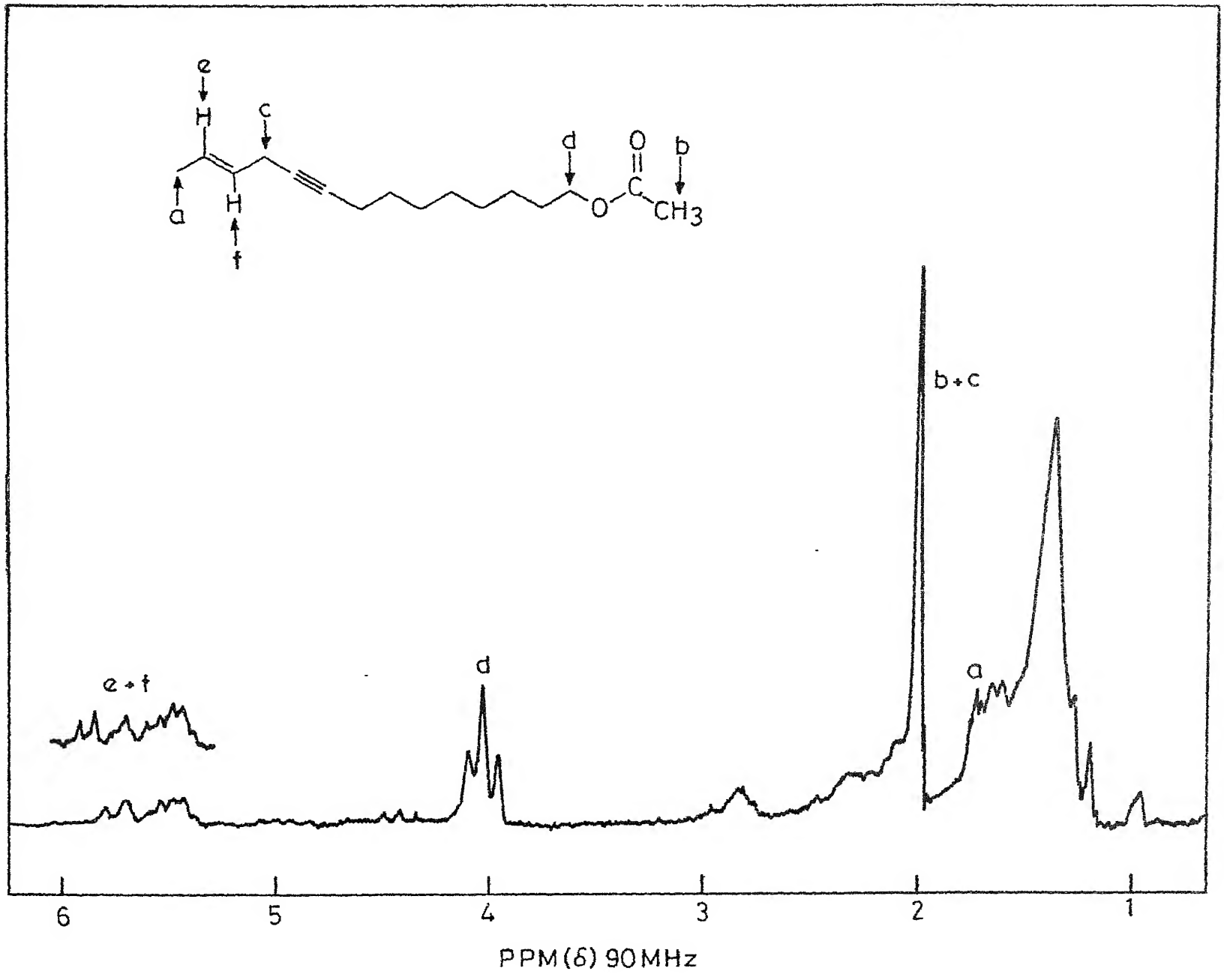

a
f
g
H
H
c
d
e
O
O
b
CH3
f+g
e
b+c+d
a
6
5
4
3
2
1
PPM (δ) 90 MHz

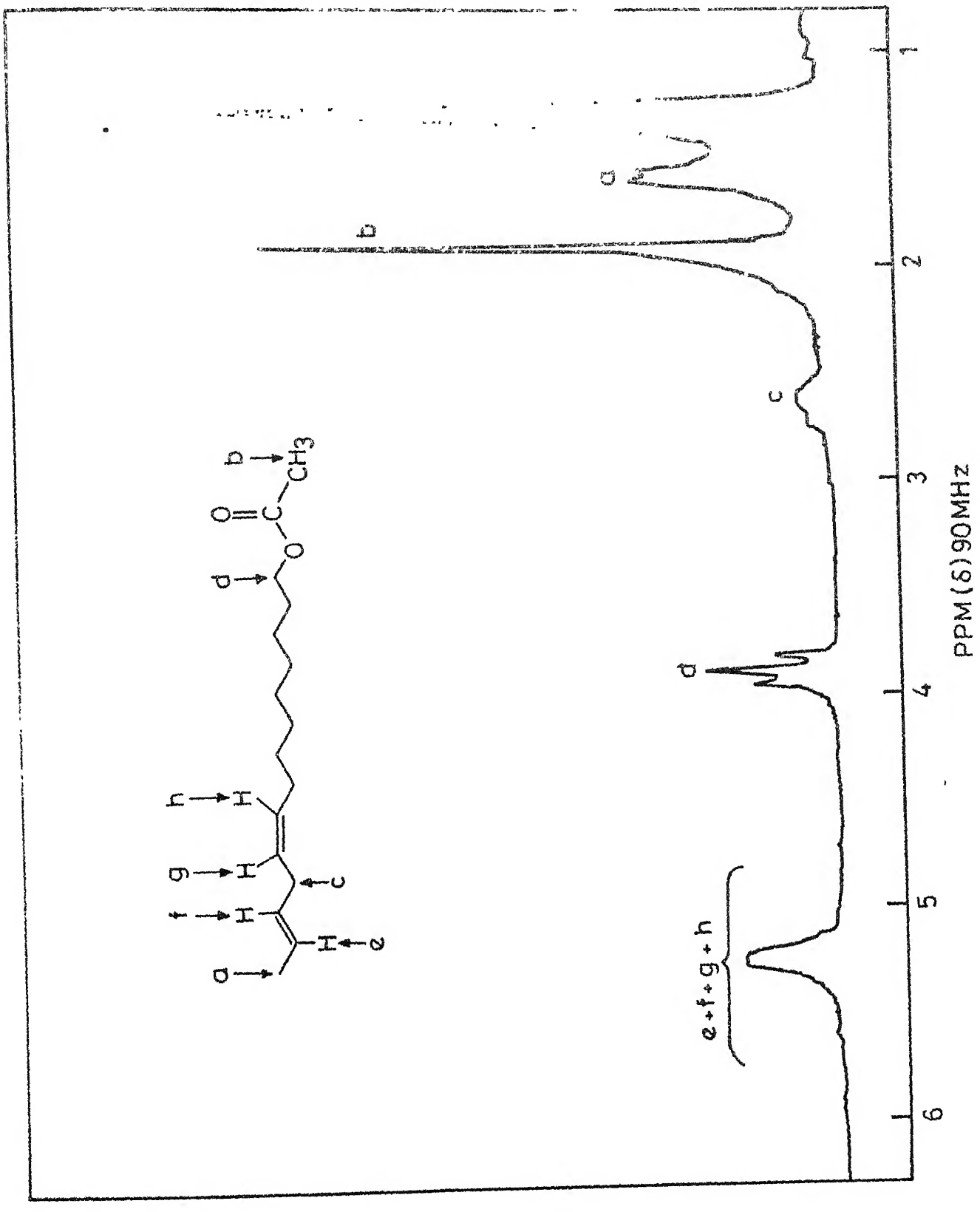

a
b+c
d+e
f
1
2
3
4
5
6
PPM (δ) 90 MHz
a
b
c
d
e
f
H
O
O
O

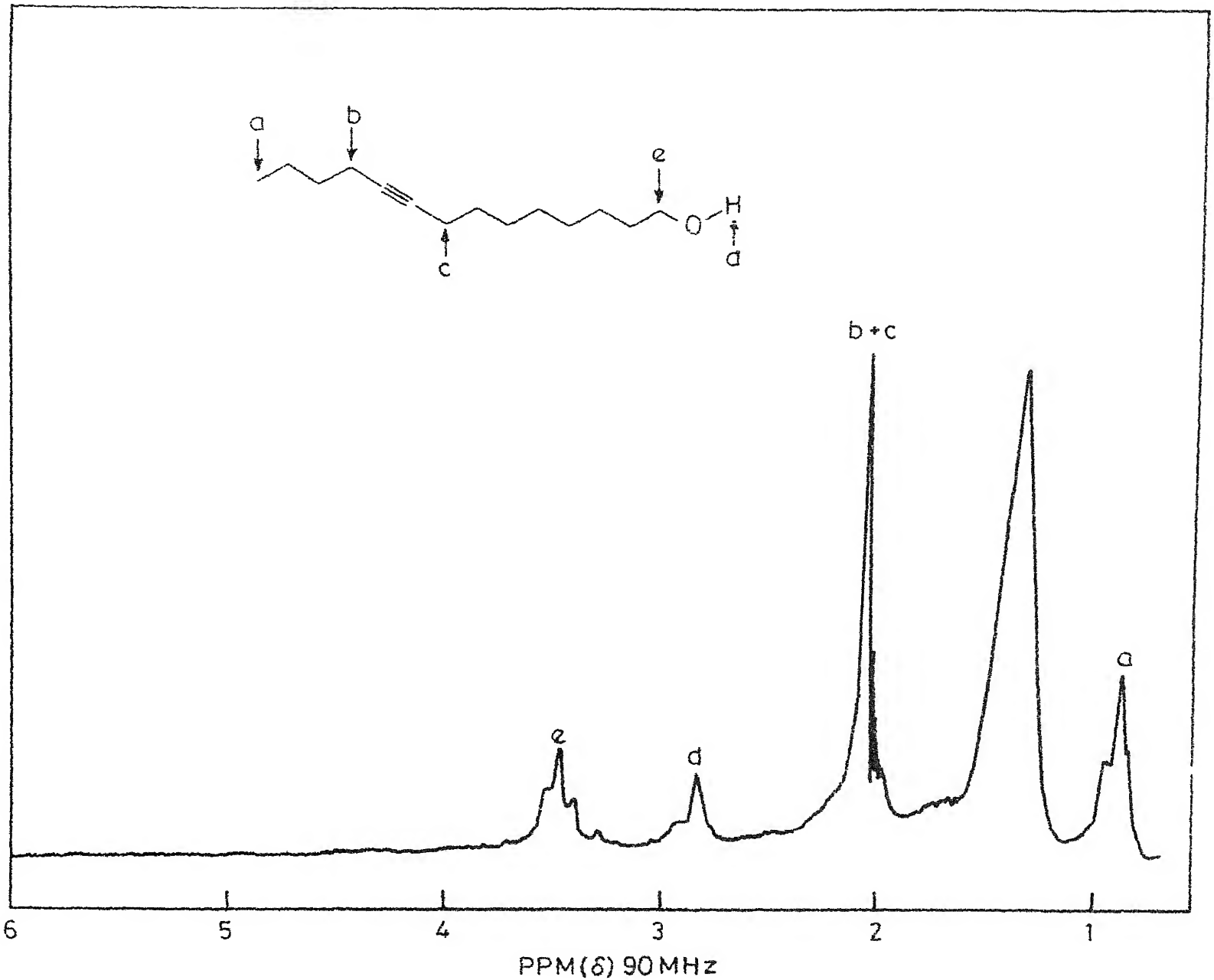

a
c
e
O
O
CH3
d
b
b
c+d
a
e
6
5
4
3
2
1
FPM(δ) 90MHz

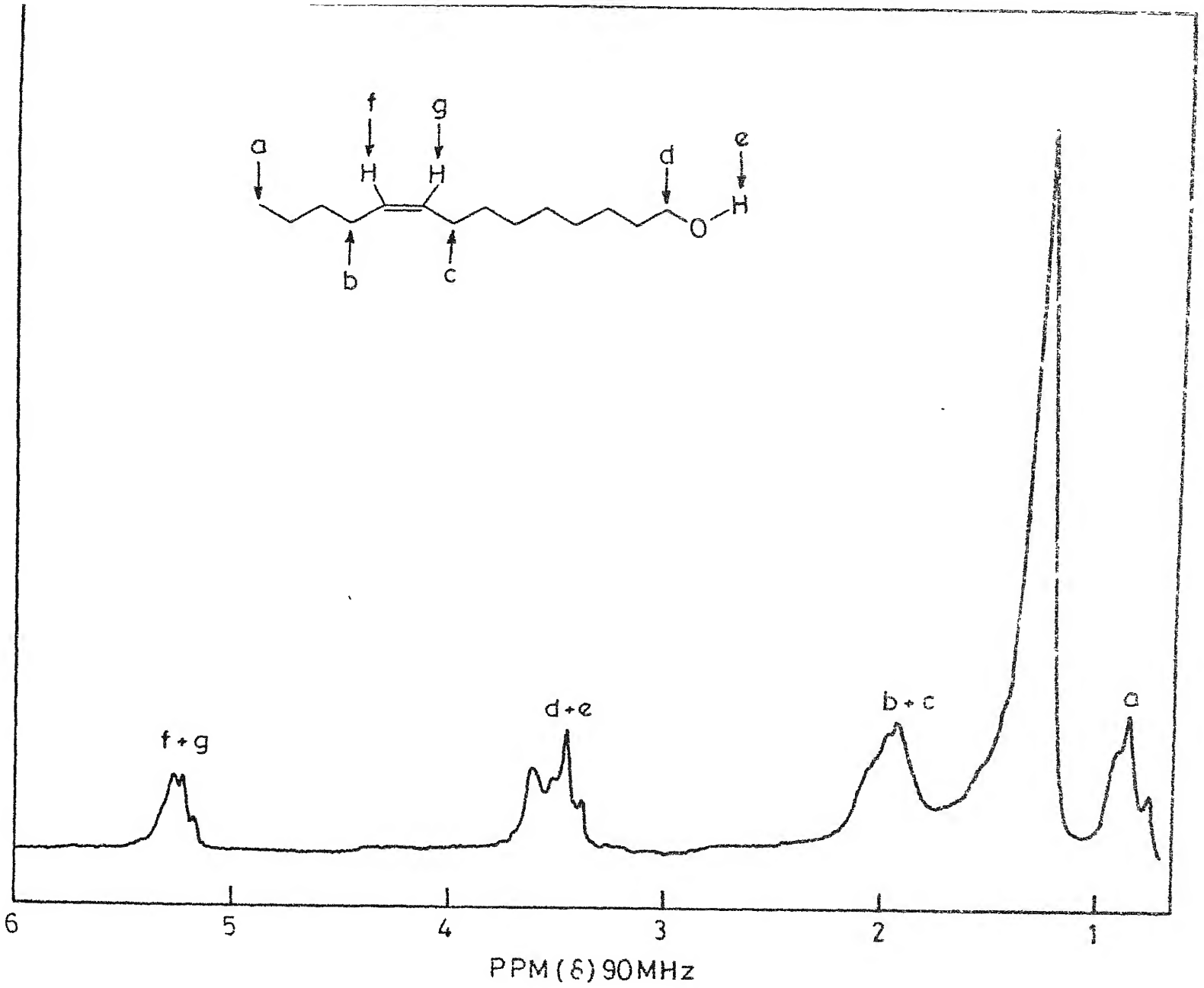

a
b
c+d
e
t+g
1
2
3
4
5
6
PPM (δ) 90MHz
a
t
H
c
g
H
d
e
O
O
b
CH3

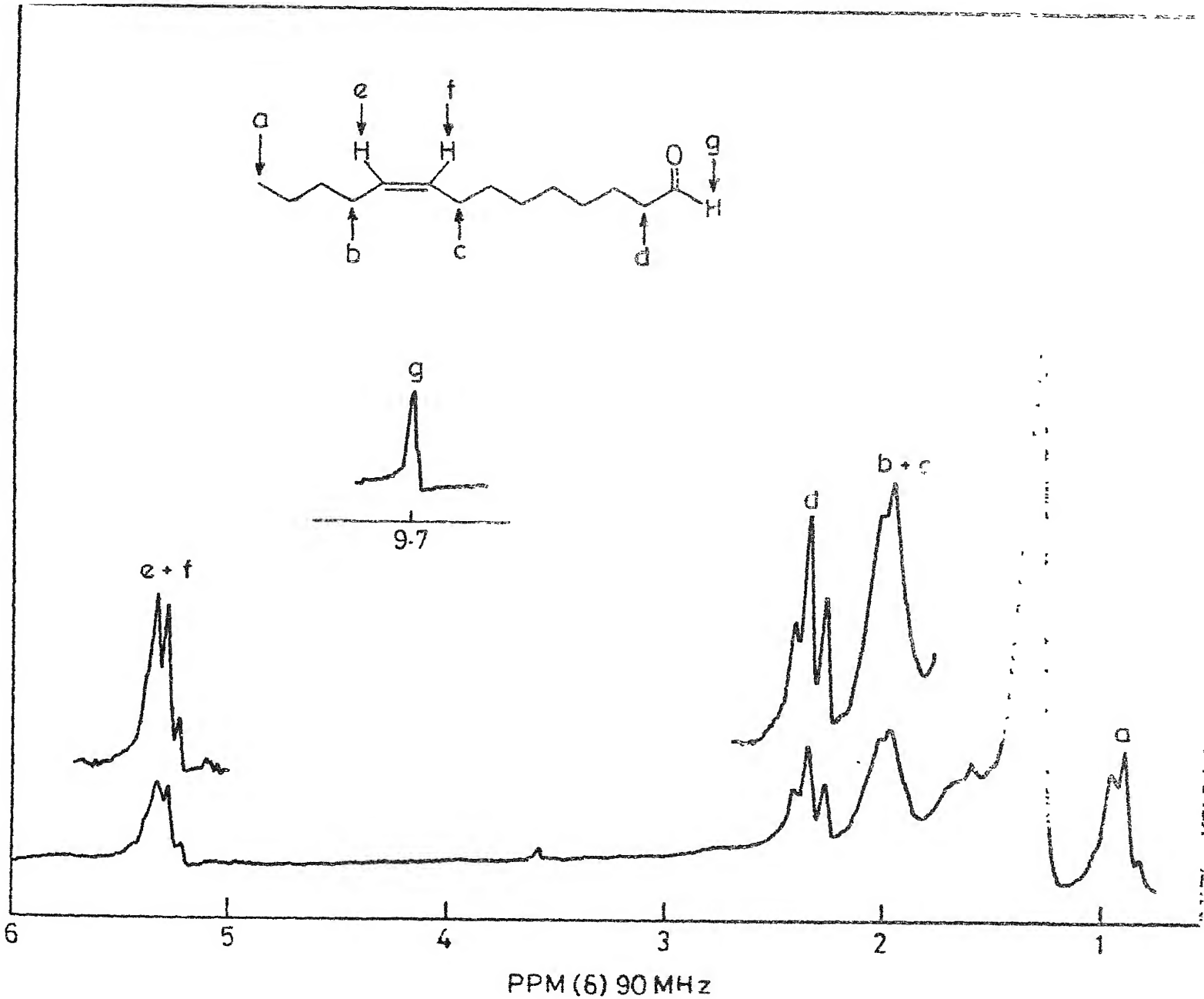

e
H
a
b
d
H
c
H
f
O
O
e+f
b+c
d
a
6
5
4
3
2
1
PPM(δ) 90MHz

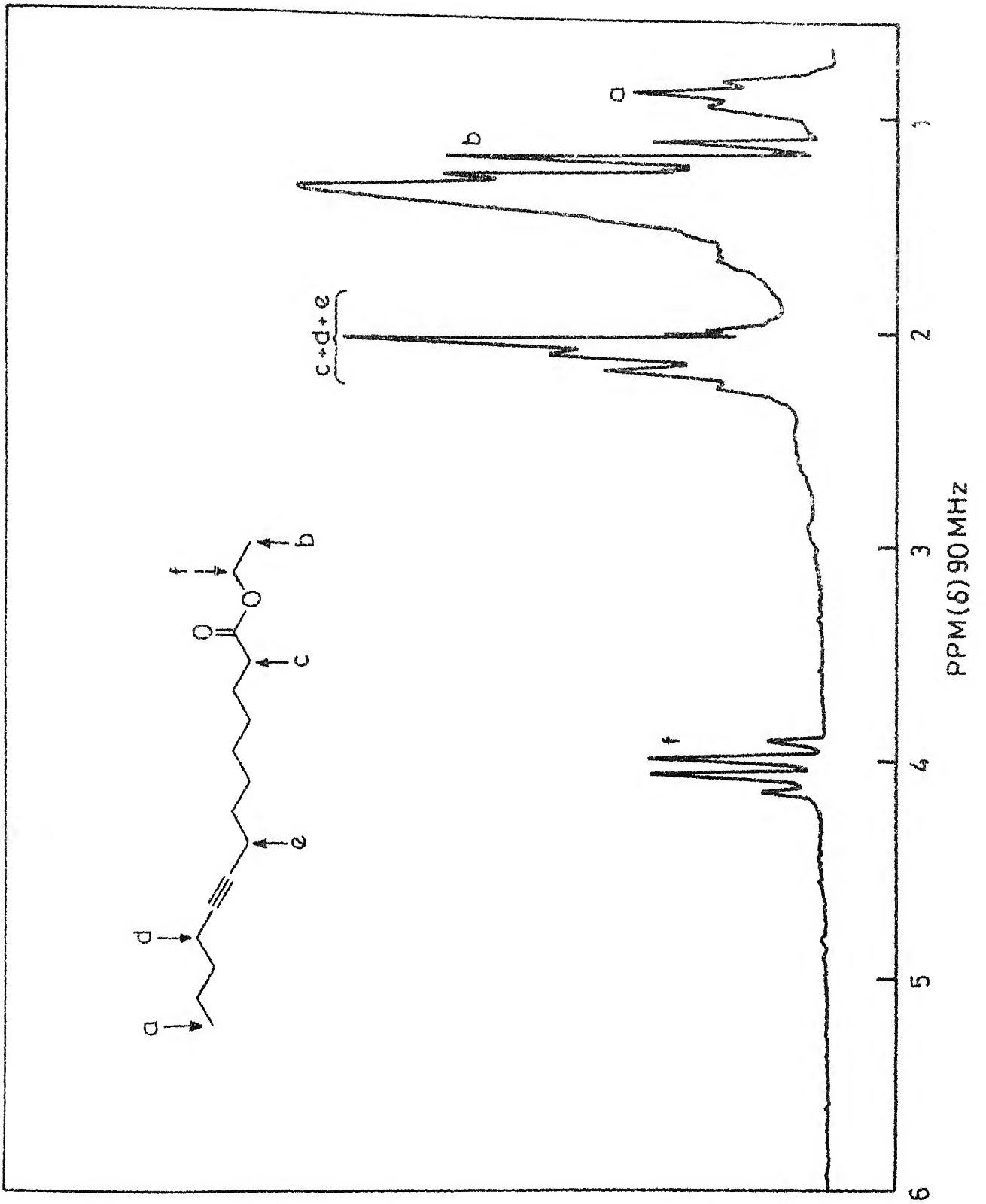

e
H
c
d
O
b
C
a
H
O
CH3
f
b+c
e+f
d
a
6
5
4
3
2
1
PPM(δ) 90MHz

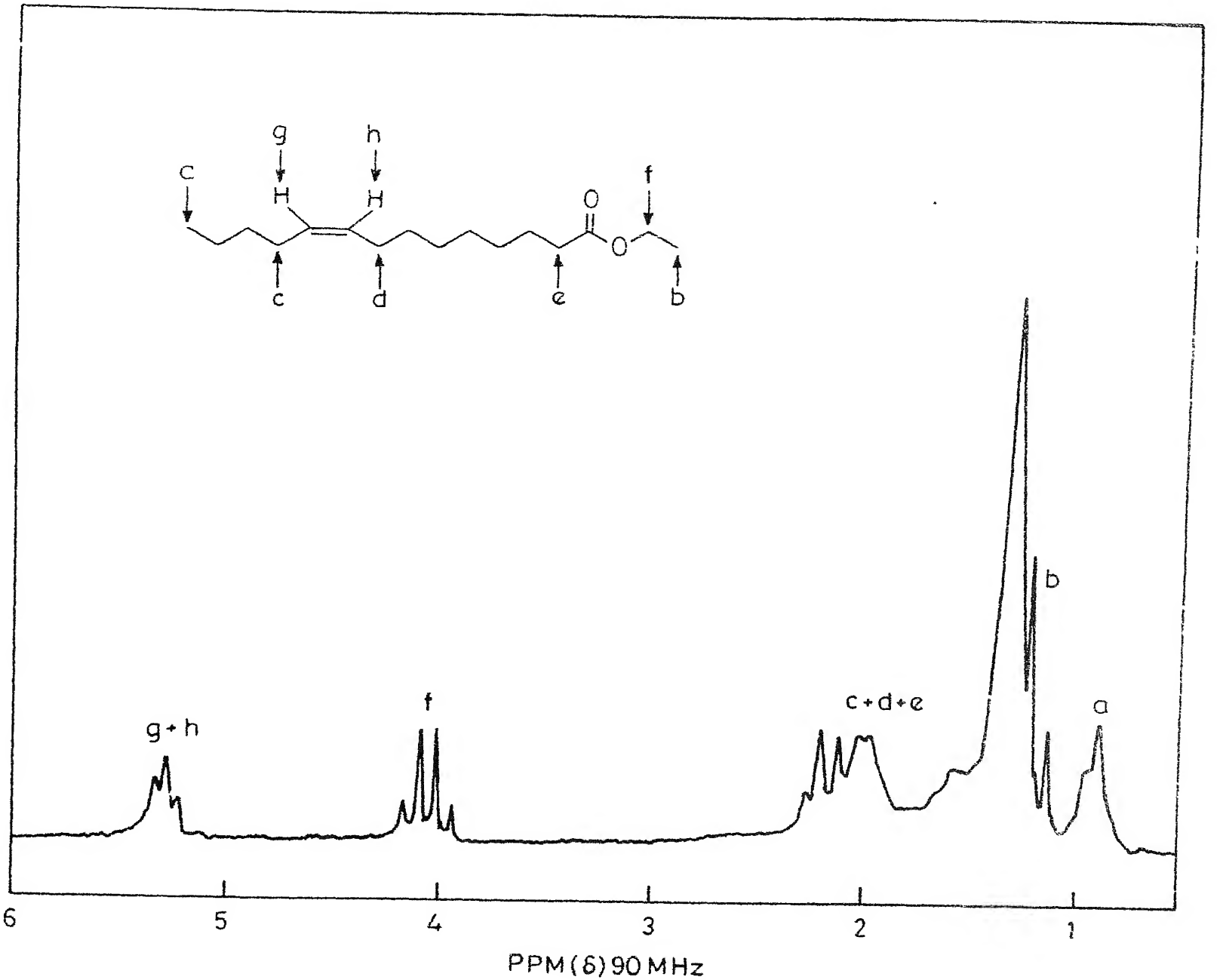

a
b
c
d
e+f+g+h
1
2
3
4
5
6
PPM(δ)90MHz
a
b
c
d
e
f
g
h
O
O
CH3

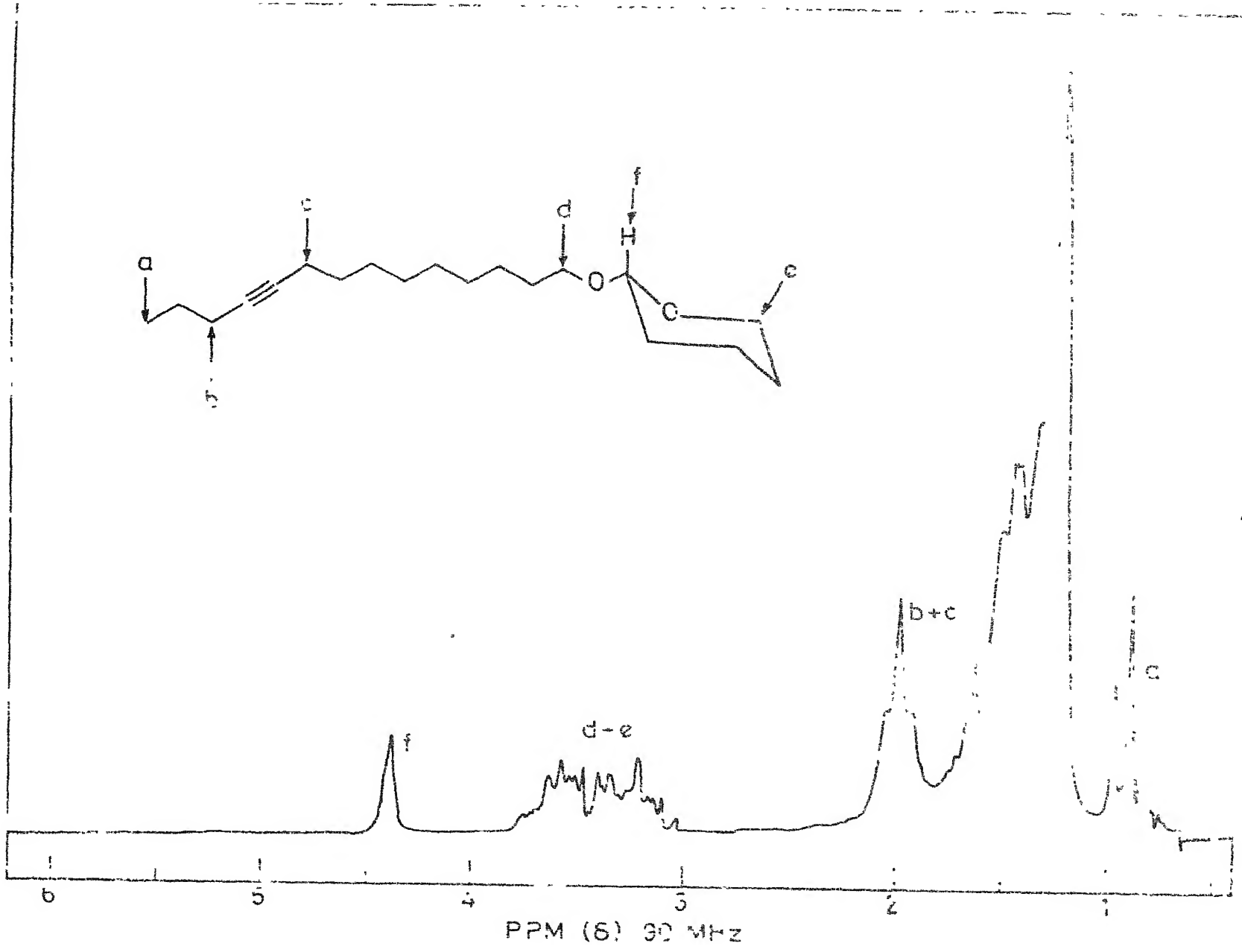

a
b
c
d
e
O
H
b+c
e
d
a
6
5
4
3
2
1
PPM(δ) 90 MHz

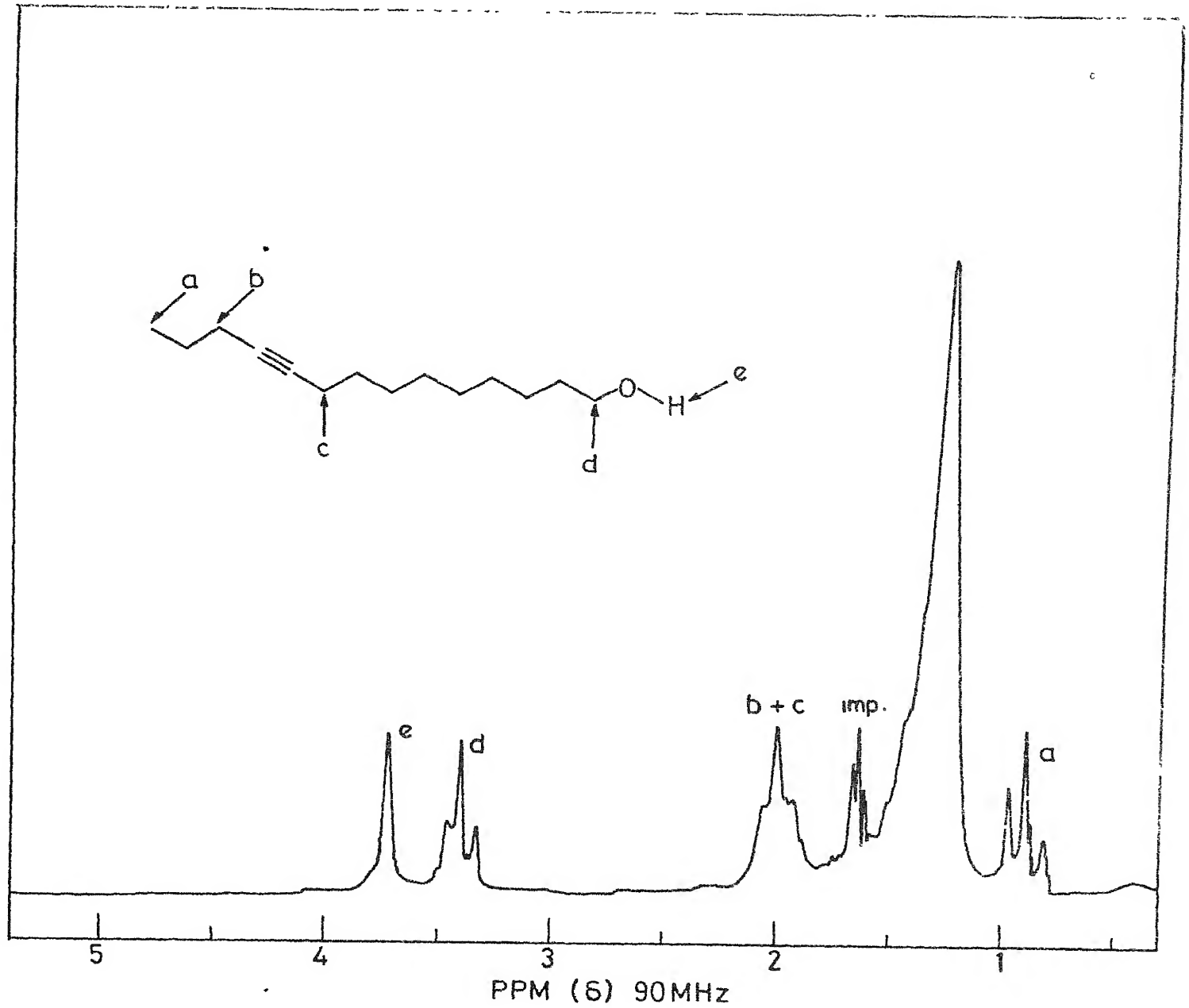

a
f
g
H
H
b
c
d
e
O
H
f + g
d + e
b + c
a
6
5
4
3
2
1
PPM (δ) 90MHz

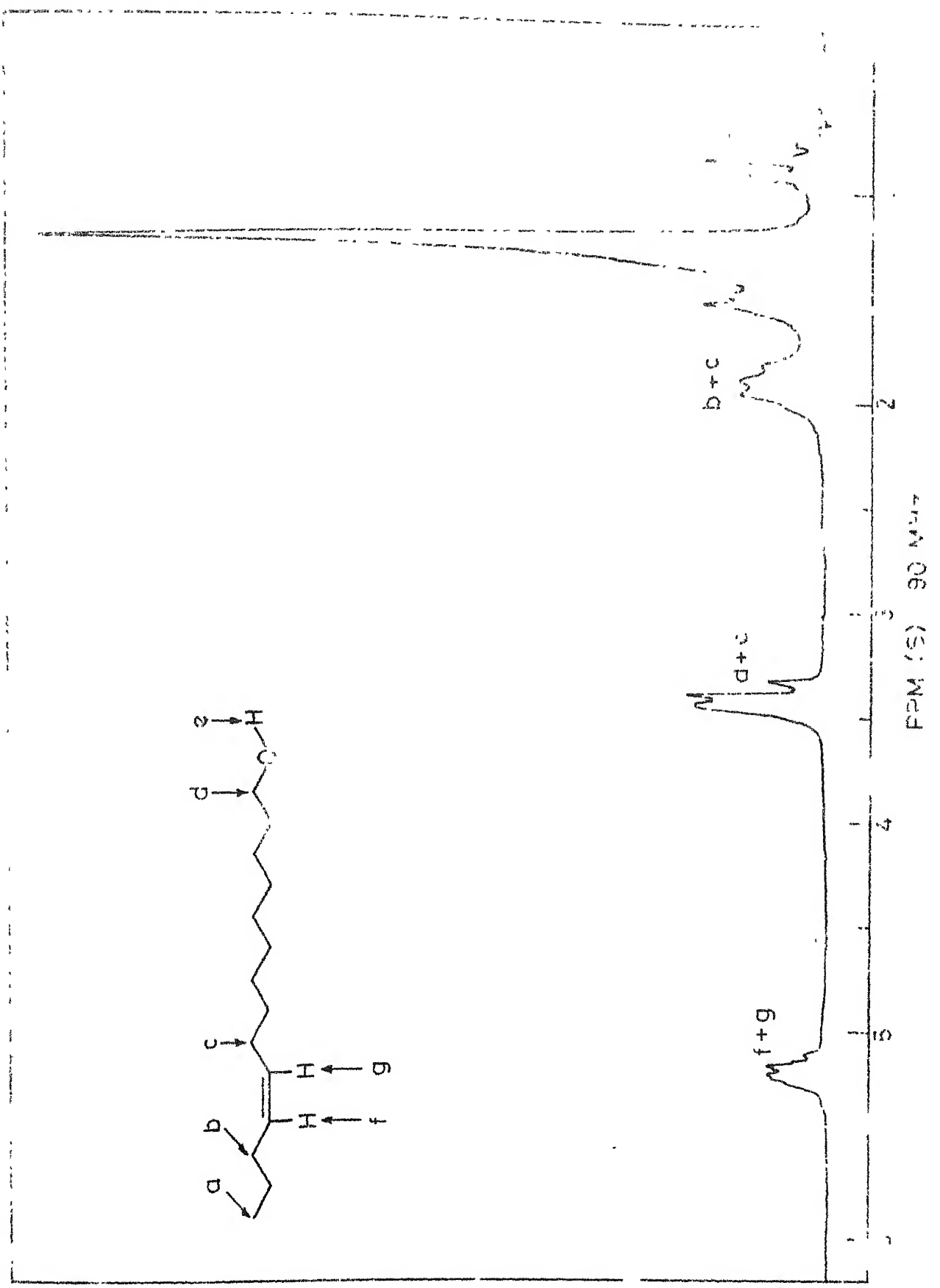

a
e
f
H
H
O
g
H
b
c
d
g
9.7
e + f
d
b + c
a
6
5
4
3
2
1
PPM (δ) 90 MHz

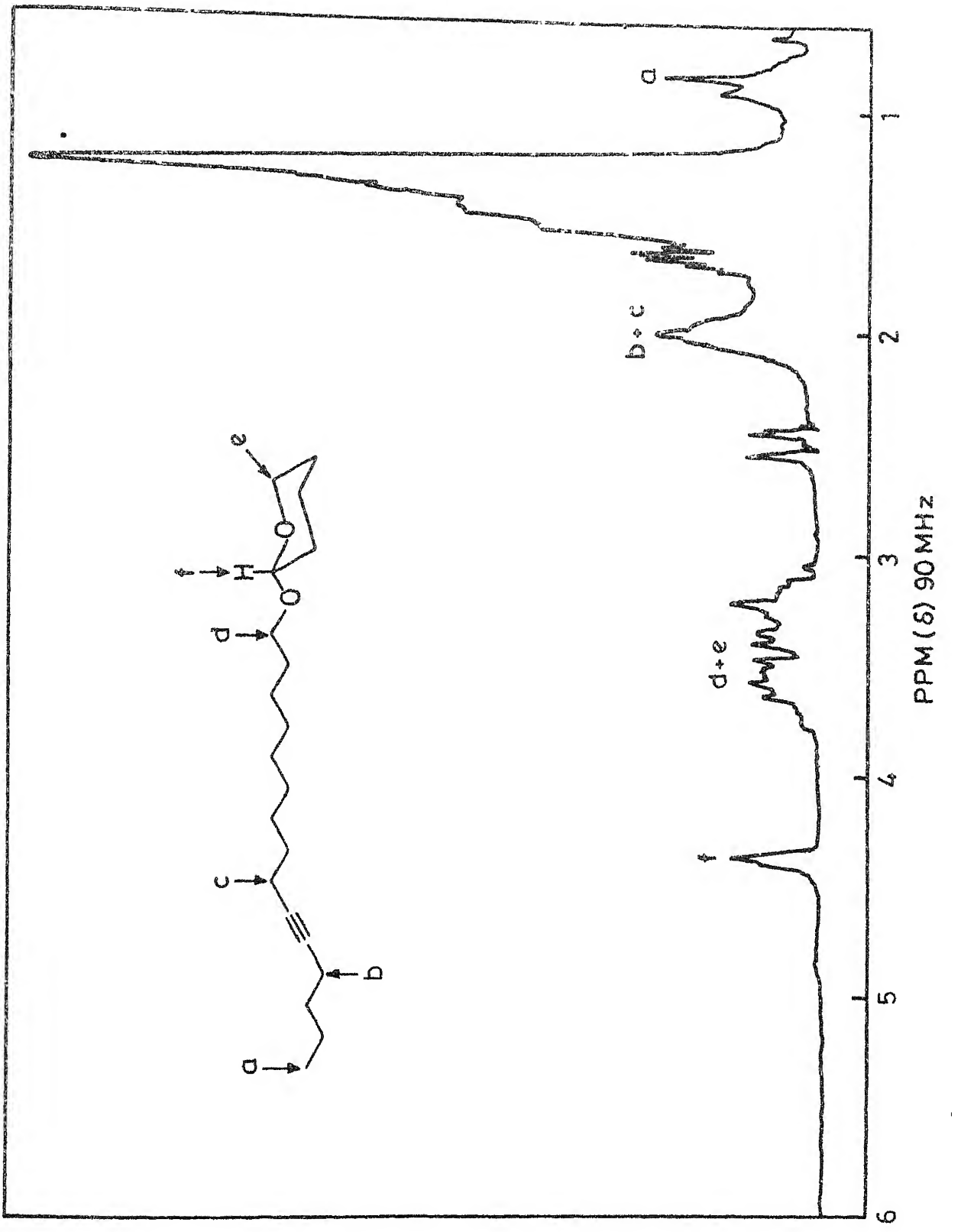

a
b
c+d+e
f
1
2
3
4
5
6
PPM(δ) 90 MHz
a
d
e
c
O
O
f
b

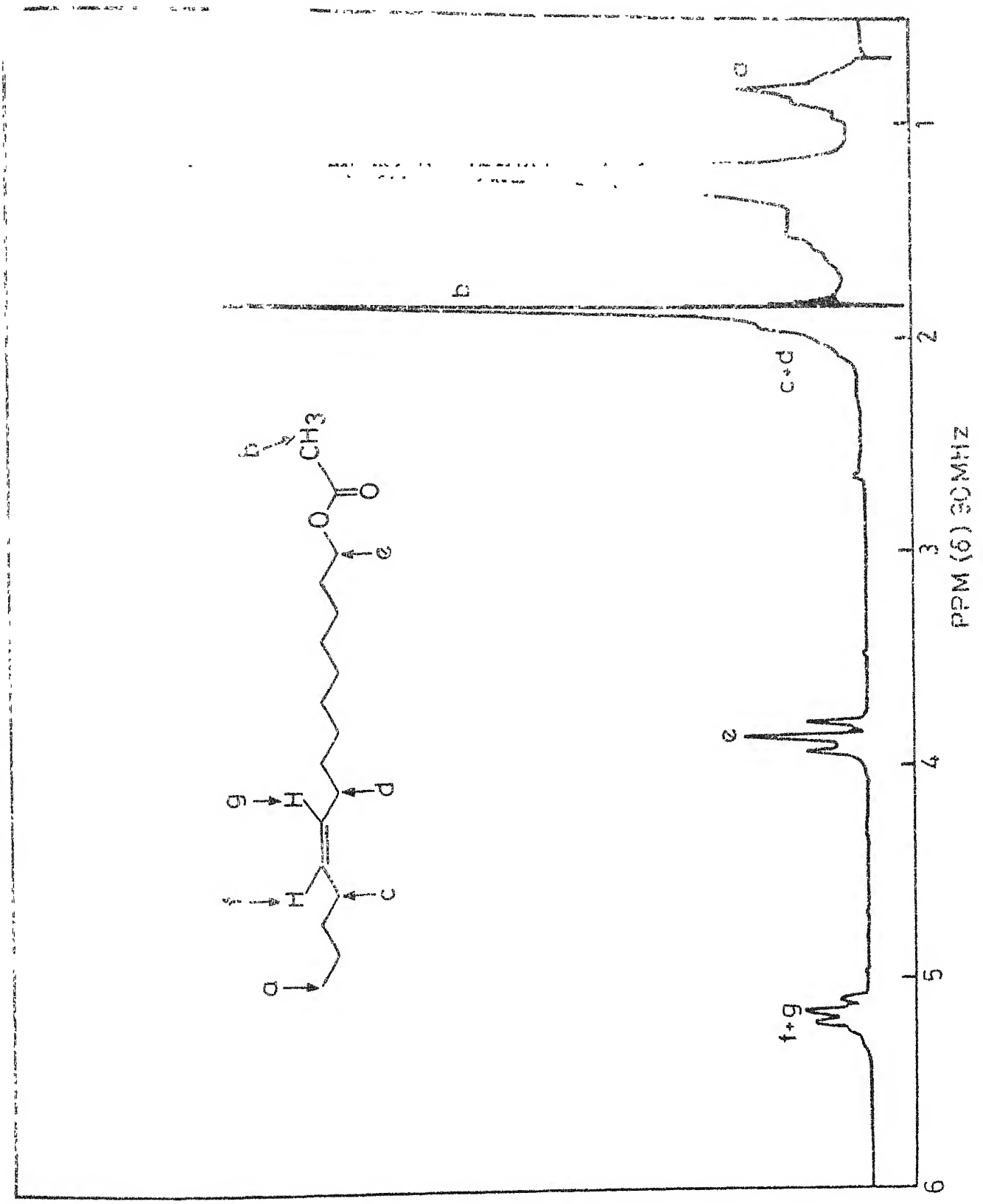

g
h
c
H
H
O
O
f
c
d
e
b
g+h
f
c+d+e
b
a
6
5
4
3
2
1
PPM(δ) 90 MHz

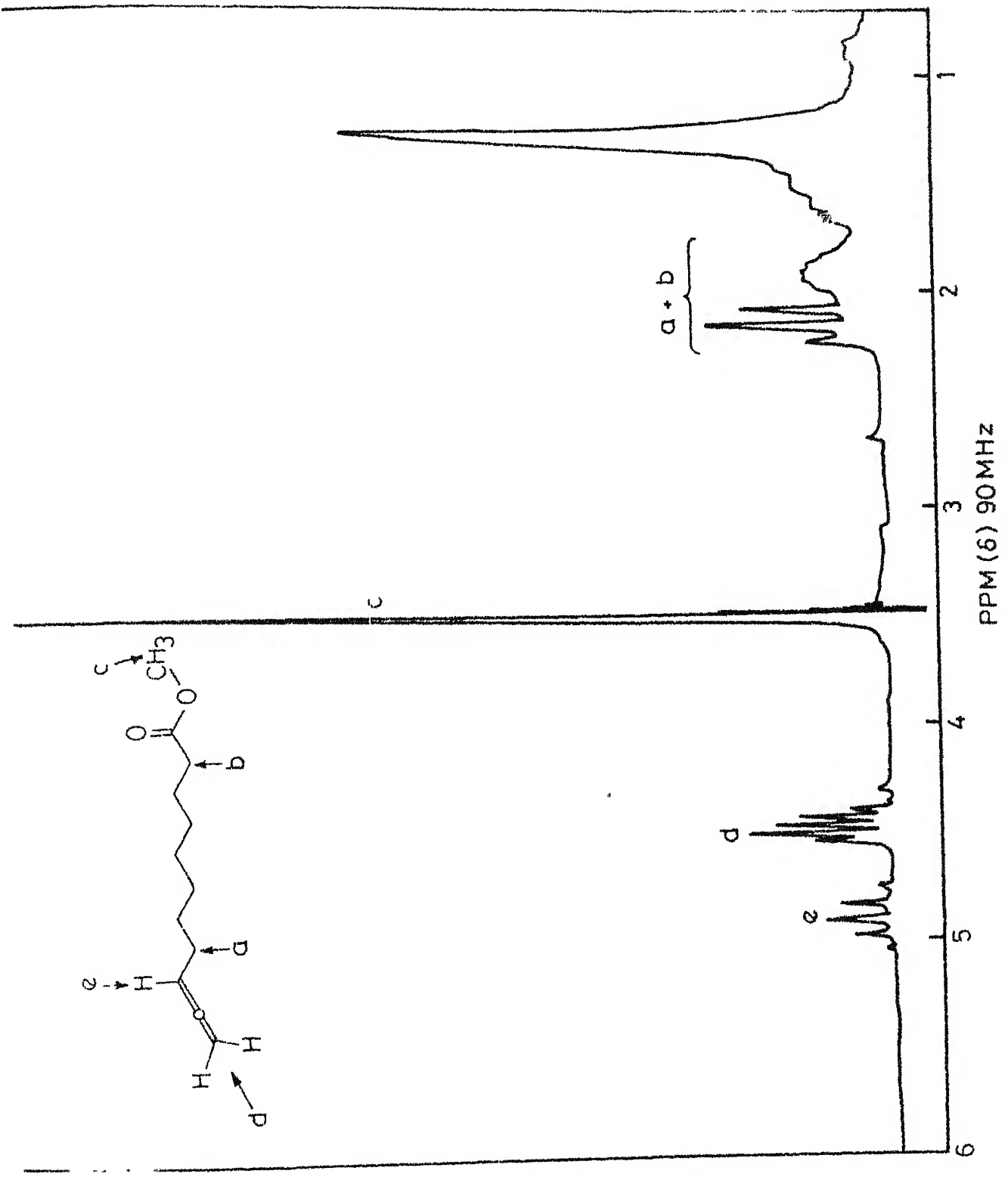

a
b
c
d
e
f
H
O
C
f
d-e
b+c
a
6
5
4
3
2
1
PPM (δ) 90 MHz


a
b
c
d
e
O
H
e
d
b + c
imp.
a
5
4
3
2
1
PPM (δ) 90MHz


a
b+c
d+e
f+g
PPM (δ) 60 MHz
1
2
3
4
5
a
a
c
H
H
g
f
e
d
d


a
b+c
d+e
f
1
2
3
4
5
6
PPM(δ) 90 MHz
a
b
c
d
e
H
O
O


a
b
c+d
e
f+g
PPM (δ) 80MHz
1
2
3
4
5
6
CH3
O
O
H
H
a
b
c
d
e
f
g


a + b
c
d
e
PPM (δ) 90MHz
1
2
3
4
5
6
c
CH3
O
O
b
d
e
H
H
H
a

I.E. EXPERIMENTAL

Melting points and boiling points are uncorrected. Infrared spectra were recorded on Perkin-Elmer, Model-377 and Perkin-Elmer Model-580 spectrophotometers as thin films for liquids and KBr discs for solids. NMR spectra were obtained on approximately 10-15% solutions in $CDCl_3$ and CCl_4 on R-32, TR-90, Bruker 80 and 270 MHz spectrometers. The chemical shifts are reported in parts per million downfield from tetramethylsilane at 0.00 as internal standard. Silica gel G (ACME) was used for thin layer chromatography and column chromatography was done on silica gel (ACME, 100-200 mesh), columns were prepared from its slurry in petroleum ether (60-80^{o}). Reactions were monitored, wherever possible, by tlc.

The transformation of castor oil upto synthons 7 and 15 was carried out by procedures reported from our laboratory (Tetrahedron 36, 1869 (1980)) with substantial improvements in some cases. The observed physical data (IR, NMR, MS) of the compounds involved are in excellent accord with that reported.

I. Trans-esterification of castor oil: Preparation of methyl 12-hydroxy (Z)9-octadecenoate (methyl ricinoleate) (1)

Sodium (1g, 0.043g atom) was added to dry methanol (3.5 l) followed by castor oil (932g, 1 mol). The reaction mixture was refluxed for 1 hr, solvents evaporated, the residue washed with MeOH:H_2O::1:1 (300 ml), the upper layer of 1 dried ($MgSO_4$) and distilled, bp 128-30°/0.02 torr; yield 795.6g (85%).

ir : ν_{max}(neat)(cm^{-1}): 3570 (hydroxyl), 1740 (ester)

nmr: $\delta_{(CDCl_3)}$: 5.45 (m, 2H, olefinic), 3.65(s, 3H, $-COOCH_3$).

II. Thermolysis of methyl ricinoleate: Isolation of methyl undec 10-enoate (2) and n-heptaldehyde (3)

Under a set-up for downward distillation, methyl ricinoleate (1) (100g), evenly supported on clean sand (25g) was heated by a Bunsen burner on a luminous flame for 0.75 hr, during which 87.0g of a light green distillate was collected. The small amount of water that came over was separated and the remainder on distillation gave heptaldehyde (3)11.3g (152°/1 atm), methyl undec 10-enoate (2) (12.0g, 49%, bp 80-81°/0.9 torr) and unchanged 1 (60.0g) which was usually recycled.

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1655 (double bond)

nmr: $\delta_{(CDCl_3)}$: 5.8 (m, 1H, olefinic), 5.0 (m, 2H, olefinic), 3.65 (s, 3H, ester).

III. Isomerisation of methyl 10-undecenoate (2) to methyl(E)9-undecenoate (4)

A vigorously stirred mixture of methyl 10-undecenoate (2) (50.0g, 0.252 mol), para-toluene sulphonic acid (5g) and dry benzene (50 ml) was refluxed for 10 hr, solvents evaporated and the residue on distillation gave 47.5g (96%) of the isomerised olefin 4, bp 79-80°/0.8 torr. The isomerisation can easily be monitored by NMR.

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1640, 970 (double bond).

nmr: $\delta_{(CDCl_3)}$: 5.4 (m, 2H, olefinic), 3.65 (s, 3H,-$COOCH_3$).

IV. Reaction of methyl(E) 9-undecenoate (4) with $Hg(OAc)_2$: Regioselective preparation of allyl acetate 5

A vigorously stirred mixture of methyl 9-undecenoate (4) (89.1g, 0.45 mol), a fresh sample of mercuric acetate (213.43g, 0.67 mol) and glacial acetic acid (200 ml), was refluxed for 15 hr, (bath temp. 120°), decanted, evaporated, diluted with water (200 ml), extracted with ether (3 x 100 ml), the ether extracts washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to yield 105g of crude 5. Fractionation gave 69.2g (86%) of 5, bp 115°/0.2 torr and 27.0g unchanged 4.

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1730 (acetate).

nmr: $\delta_{(CDCl_3)}$: 5.65 (m, 2H, olefinic), 4.5 (d, J = 5Hz, 2H, -CH_2-OAc), 3.65 (s, 3H, -$COOCH_3$), 2.0(s,3H,-$OCOCH_3$).

V. Trans-esterification of 5: Isolation of allylic alcohol 6

A solution of methyl 11-acetoxy (E) 9-undecenoate (5), (57.0g, 0.22 mol), in dry methanol (75 ml) was added to a stirred suspension of freshly ignited potassium carbonate (56.5g, 0.33mol) in dry methanol (40 ml). The reaction mixture was left stirred for 2 hr, decanted, solvents evaporated under reduced pressure, the residue neutralized with ice cold HCl (2N), extracted repeatedly with dichloromethane (5 x 100 ml), the organic extract washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to yield 46g of crude 6 which was distilled, bp 120-121°/0.07 torr; yield 43.9g (92%).

ir : ν_{max}(neat)(cm^{-1}): 3640 (hydroxyl), 1740 (ester).

nmr: $\delta_{(CDCl_3)}$: 5.6 (m, 2H, olefinic), 4.0 (br, 2H, $-C\underline{H}_2-OH$), 3.65 (s, 3H, $-COOC\underline{H}_3$).

VI. Oxidation of allylic alcohol 6: Vastly improved preparation of key synthon 7

a. Preparation of Pyridinium dichromate (PDC)

Pyridine (80.6 ml) was gradually added to a solution of CrO_3 (100g, 1 mol) in water (100 ml), maintaining the temperature below 30°. The reaction mixture was diluted with acetone (400 ml), cooled ($\sim$-20°) for 3 hr, the orange crystals of PDC collected, washed with acetone and dried *in vacuo*. Yield 127.0g (68%).

b. Oxidation of allylic alcohol 6

A solution of the allylic alcohol 6 (1.06g, 5 mmol) in dry dichloromethane (5 ml) was added to a well stirred suspension of PDC (2.92g, 7.5 mmol) in dry dichloromethane (5 ml). The reaction mixture was left stirred for 24 hr at 25°, diluted with ether (100 ml), the ether extract passed through a small column of anhydrous $MgSO_4$ and evaporated to give 0.888g (84%) of aldehyde 7 , bp 105-110°/0.06 torr.

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1690 (aldehyde), 1660 (double bond).

nmr: $\delta_{(CDCl_3)}$: 9.4 (d, J = 9Hz, 1H, -CHO), 6.9 (m, 1H, olefinic), 6.1 (m, 1H, olefinic), 3.68 (s, 3H,-$COOCH_3$).

Semicarbazone: mp 139-140°.

ir : ν_{max}(KBr)(cm^{-1}): 3280 (-NH), 1740 (ester), 1695(amide), 1655 (double bond).

nmr: $\delta_{(CDCl_3)}$: 9.9 (br, 1H, -CH=N-), 7.5 (br, 1H,-NH), 6.2 (br, 2H, -$CONH_2$), 5.8 (br, 2H, olefinic), 3.75 (s, 3H, -$COOCH_3$).

VII. Degradation of methyl 10-undecenoate (2) to methyl 9-decenoate (11)

a. Addition of PhMgBr to 2: Isolation of adduct 8

To a well stirred solution of PhMgBr [from 12.15g Mg (0.5g atom) and 78.5g (0.5 mol) of bromobenzene] in ether (500 ml) was added, in drops, over 1 hr, keeping the temperature below 20°, a solution of methyl undec 10-enoate (2), (50.0g, 0.25 mol) in ether (500 ml). The mixture was refluxed for 2.5 hr, the Grignard complex decomposed with ice-cold 2N H_2SO_4, extracted with ether, washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to yield 77.0g (95%) of alcohol 8 which was used without purification in the following experiment.

ir : ν_{max} (neat) (cm^{-1}): 3595 (hydroxyl), 1655 (double bond), 1610 (phenyl).

b. Dehydration of alcohol 8: Isolation of diene 9

Neat alcohol 8 (77.0g) was held at 200° for 0.5 hr and fractionated to give 60.0g (78%) of 9, bp 163-165°/0.07 torr.

ir : ν_{max} (neat) (cm^{-1}): 1655 (double bond), 1610 (phenyl).

nmr: $\delta_{(CDCl_3)}$: 7.2 (m, aromatic), 5.85 (m, 1H, olefinic), 5.0 (m, 2H, olefinic).

c. Oxidation of diene 9: Preparation of 9-decenoic acid (10)

To a vigorously stirred solution of 9 (18.0g, 0.059 mol) in glacial acetic acid (250 ml) was added, in drops, over 1.5 hr a solution of chromium trioxide (14.0g, 0.14 mol) in water (20 ml) [CAUTION: The reaction is very exothermic ! The inside temperature should not exceed 35°]. After an additional 0.5 hr stirring, the reaction mixture was treated with ice-cold 2N H_2SO_4 (0.75 l), extracted with benzene (5 x 100 ml) and evaporated. The residue was triturated with satd. $NaHCO_3$, extracted with ether (2 x 100 ml), the aqueous layer carefully acidified with ice cold 2N HCl, extracted with ether (3 x 100 ml), the organic layer washed with brine, dried ($MgSO_4$) and evaporated to give 6.6g (66%) of 10, bp $93-95^{\circ}/0.8$ torr.

ir : ν_{max}(neat)(cm^{-1}): 1710 (carboxyl), 1655 (double bond).

nmr: δ ($CDCl_3$): 5.8 (m, 1H, olefinic), 5.0 (m, 2H, olefinic).

d. Fischer esterification of 9-decenoic acid (10): Preparation of methyl 9-decenoate (11)

A solution of 9-decenoic acid (10) (26.5g, 0.15 mol) in dry methanol (250 ml) was admixed with conc. H_2SO_4 (0.5 ml) and refluxed for 2 hr. Methanol was distilled off, the residue poured into ice-cold water (500 ml), the upper oily layer extracted with ether (3 x 100 ml), washed with satd. $NaHCO_3$, brine,

dried ($MgSO_4$) and evaporated to give 28g (98%) of methyl dec 9-enoate (11), bp 60-61°/0.3 torr.

ir : ν_{max}(neat) (cm^{-1}): 1740 (ester), 1655, (double bond).

nmr: $\delta_{(CDCl_3)}$: 5.8 (m, 1H, olefinic), 4.9 (m, 2H, olefinic), 3.68 (s, 3H, $-COOCH_3$).

VIII. Isomerisation of methyl 9-decenoate (11): Preparation of methyl (E) 8-decenoate (12)

The isomerisation of 11 was done as outlined for the related 2 ⟶ 4 change (Experiment III). A mixture of 11 (25g, 13.5 mmol), para-toluene sulphonic acid (2g) and dry benzene (50 ml), was refluxed for 10 hr. Work up, as described in Experiment III, gave 24.3g (97%) of methyl (E) 8-decenoate (12), bp 60-61°/0.2 torr.

ir : ν_{max}(neat) (cm^{-1}): 1740 (ester), 1640, 970 (double bond).

nmr: $\delta_{(CDCl_3)}$: 5.4 (m, 2H, olefinic), 3.65 (s, 3H, $-COOCH_3$).

IX. Reaction of 12 with $Hg(OAc)_2$: Regioselective preparation of allyl acetate 13

The allylic acetoxylation was carried out as described in Experiment IV, for the 4 ⟶ 5 change. A mixture of 12 (22.5g, 0.12 mol), a fresh sample of mercuric acetate (58g, 0.18 mol) and glacial acetic acid (100 ml) was refluxed for 15 hr. Work-up,

as outlined in Experiment IV gave 16.5g (85%) of 13, bp 115°/ 0.13 torr and 7.3 g of unchanged 12.

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1730 (acetate).

nmr: $\delta_{(CDCl_3)}$: 5.65 (m, 2H, olefinic), 4.5 (d, J = 5 Hz, 2H, $-C\underline{H}_2OAc$), 3.65(s, 3H, $-COOC\underline{H}_3$), 2.0 (s, 3H, $-COC\underline{H}_3$).

X. Trans-esterification of acetate 13: Isolation of allylic alcohol 14

The trans esterification of acetate 13 was performed as described in Experiment V for the 5 ⟶ 6 change. To a well stirred suspension of freshly ignited potassium carbonate (20.7g, 0.55 mol) in dry methanol (30 ml) was added a solution of 13 (30g, 0.124 mol) in dry methanol (25 ml). The reaction mixture was left stirred for 2 hr. Work-up, as described in Experiment V, gave 23.3g (94%) of methyl 10-hydroxy (E) 8-decenoate (14), bp 115°/ 0.04 torr.

ir : ν_{max}(neat)(cm^{-1}): 3640 (hydroxyl), 1740 (ester).

nmr: $\delta_{(CDCl_3)}$: 5.65 (m, 2H, olefinic), 4.0 (br, 2H, $-C\underline{H}_2-OH$), 3.65 (s, 3H, $-COOC\underline{H}_3$).

XI. Oxidation of allyl alcohol 14: Vastly improved preparation of the key synthon 15

The oxidation was carried out as described for the 6 ⟶ 7 change in Experiment VI. A solution of the allylic alcohol 14 (1g, 5 mmol) in dry dichloromethane (5 ml) was added to a well stirred suspension of PDC (2.92g, 7.5 mmol) in dry dichloromethane (5 ml). The reaction mixture was left stirred for 24 hr at 25°. Work-up as described in Experiment VI gave 0.807g (81.5%) bp 108-113°/0.1 torr.

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1690 (aldehyde), 1640 (double bond).

nmr: $\delta_{(CDCl_3)}$: 9.4 (d, J = 9 Hz, 1H, -CHO), 6.75 (m, 1H, olefinic), 5.8 (m, 1H, olefinic), 3.65 (s, 3H,-$COOCH_3$).

Semicarbazone: mp 130-131°

ir : ν_{max}(KBr)(cm^{-1}): 3280 (-NH), 1740 (ester), 1690(amide), 1655 (double bond).

nmr: $\delta_{(CDCl_3)}$: 9.88 (br, 1H, -CH=N-), 7.50 (br, 1H, -NH), 6.20 (br, 2H, -$CONH_2$), 5.78 (br, 2H, olefinic), 3.78 (s, 3H, -$COOCH_3$).

XII. Synthesis of (E) 9,11-dodecadien 1-ol acetate (18): The pheromone of red bollworm moth

a. Preparation of triphenylmethylphosphonium bromide

Sulfuric acid (95% , 100 ml) was added cautiously to ice-cooled and stirred methanol (80g, 2.5 mol). Half of the resultir solution was added to sodium bromide crystals (120g, 1.165 mol) and the reaction mixture heated on a water bath. The remaining half of the MeOH:H_2SO_4 solution was then slowly added. Methyl bromide generation was brisk and continuous. It was passed through potassium hydroxide, collected at -5° and added to an ice-salt cooled solution of triphenylphosphine (55g, 0.21 mol) in dry benzene (45 ml), which was sealed and left aside overnight to give 74.5g (99%) of the crystalline phosphonium salt. The crude product was washed thoroughly with hot dry benzene (500 ml) dried at 120° for 8 hr and then in vacuo over P_2O_5. mp 230-31° (lit. 232-3°); yield 73.4g (98%).

b. Reaction of 7 with triphenylmethylphosphonium bromide: Isolation of methyl (E) 9,11-dodecadienoate (16)

Under nitrogen, to a stirred suspension of NaH (210 mg, 4.4 mmol; 50% dispersion in oil) in dimethoxyethane (20 ml), was added, in one lot, 1.563g (4.4 mmol) of triphenylmethylphosphoni bromide and the mixture refluxed for 1 hr during which a yellow precipitate appeared. The reaction mixture was raised from the

hot oil bath, a solution of 7 (0.936g, 4.4 mmol) in DME (10 ml) was added in drops and reflux continued for 2 hr. The reaction mixture was neutralised with AcOH, solvents evaporated *in vacuo*, the residue extracted with ether, the organic extract washed with water, 10% $NaHCO_3$, brine, dried ($MgSO_4$), solvents evaporated and the residue chromatographed over silica gel. Elution with petroleum ether:benzene::20:80 gave 0.501g (52.8%) of diene ester 16.

Anal. Calcd. for $C_{13}H_{22}O_2$ (Mol. Wt. 210)
C, 74.28; H, 10.47%
Found C, 74.59; H, 10.2 %

ir : ν_{max}(neat) (cm^{-1}): 1740 (ester), 1652, 970 (double bond).

nmr: $\delta_{(CCl_4)}$: 1.9-2.5 (m, 4H, =CH-C<u>H</u>$_2$, -C<u>H</u>$_2$COOCH$_3$), 3.7 (s, 3H, -COOC<u>H</u>$_3$), 4.6-6.6 (complex multiplet, 5H, olefinic).

c. Reaction of methyl (E) 9,11-dodecadienoate (16) with lithium aluminium hydride: Preparation of (E) 9,11-dodecadien 1-ol (17)

A solution of diene ester 16, (0.388g, 1.8 mmol) in dry ether (10 ml) was added at RT to a well stirred suspension of $LiAlH_4$ (113 mg, 3 mmol) in dry ether (15 ml). The reaction mixture was left stirred for 2 hr, excess reagent decomposed by cautious addition of cold water, extracted with ether, washed with brine, dried ($MgSO_4$), solvents evaporated and the residue

chromatographed over silica gel. Elution with benzene:ethyl-acetate::90:10 gave 0.271g (80.59%) of 9,11-dodecadien 1-ol(17).

ir : ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl), 1655, 950 (double bond).

d. Reaction of (E) 9,11-dodecadien 1-ol (17) with acetic anhydride - pyridine: Isolation of (E) 9,11-dodecadien 1-ol acetate (18), the red bollworm moth pheromone

A solution of the diene alcohol 17 (0.271g, 1.5 mmol), acetic anhydride, A.R. (2 ml) and pyridine (0.5 ml) was left aside overnight, solvents evaporated in vacuo and the residue subjected to bulb to bulb distillation; bp 105-110°/0.05 torr, yield 0.33g (99%), sample for glc analysis was made by preparative tlc using benzene as developer.

Anal. Calcd. for $C_{14}H_{24}O_2$ (Mol. Wt. 224)
C, 75.0; H, 10.71%
Found C, 74.8; H, 10.6%

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester)

nmr: $\delta_{(CDCl_3)}$: (270 MHz) 2.02(s, 3H, $-OCOC\underline{H}_3$), 4.06 (t, 2H, $-C\underline{H}_2OAc$), 4.9 (dd), 5.2 (dd)($C\underline{H}_2$=CH-), 5.8 (dt, $-CH=C\underline{H}-CH_2-$), 6.1 (q, $-CH=CH-C\underline{H}=CH-$), 6.3 (dt, $H_2C=C\underline{H}-$).

glc: (1.8 m x 2 mm i.d.)

5% 4-(p-Methoxycinnamyloxy)-4'-methoxyazobenzene,

on gaschrom Q 100-120 mesh

100° @ 2°C/min

E:Z::98.3:1.7.

XIII. Preparation of (E,E) 8,10-dodecadien 1-ol (20): The pheromone of codling moth

a. Preparation of triphenylethylphosphonium bromide

A solution of ethyl bromide (22.8g, 0.21 mol) and triphenylphosphine (55g, 0.21 mol) in dry benzene (50 ml) was sealed, left aside for 1 week, the precipitate collected, washed with hot dry benzene, dried at 120° and then *in vacuo* over P_2O_5 to give 76.6g (98.1%) of the phosphonium salt, mp 203-205° (lit. 203-4°).

b. Reaction of 15 with triphenylethylphosphonium bromide: Isolation of methyl 8,10-dodecadienoate (19)

Under nitrogen and stirring, was added, in one lot, triphenylethylphosphonium bromide (1.845g, 5 mmol) to a suspension of NaH (0.24g, 5 mmol, 50% dispersion in oil) in dimethoxyethane (20 ml). The mixture was refluxed for 1 hr when an orange-yellow precipitate appeared. The reaction mixture was

raised from the hot oil bath, a solution of 15 (0.990g, 5 mmol) in dimethoxyethane (10 ml) was introduced in drops, the reaction mixture refluxed for an additional 2 hr, neutralised with AcOH, solvents evaporated in vacuo, the residue extracted with ether, washed with 10% $NaHCO_3$, brine, dried ($MgSO_4$), solvents evaporated and the residue chromatographed on silica gel. Elution with petroleum ether:benzene::20:80 gave 0.529g (50.38%) of 19.

Anal. Calcd. for $C_{13}H_{22}O_2$ (Mol. Wt. 210)
C, 74.28; H, 10.47%
Found C, 73.79; H, 10.67%

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1655, 970 (double bond).

nmr: δ ($CDCl_3$): (270 MHz) 1.65(dd, $C\underline{H}_3$-CH=CH-), 3.65 (s, -$COOC\underline{H}_3$), 5.35 (dt, -CH=C$\underline{H}$-CH_2-), 5.5 (m, CH_3-C$\underline{H}$=CH-), 5.8 (m, CH_3-CH=C$\underline{H}$-), 6.3 (dd, -C$\underline{H}$=CH-CH_2).

c. Reaction of methyl 8,10-dodecadienoate (19) with lithium aluminium hydride: Isolation of 8,10-dodecadien 1-ol (20)- the pheromone of codling moth

A solution of methyl 8,10-dodecadienoate (19), (0.3g, 1.4 mmol), in dry ether (10 ml) was added to a well stirred suspension of $LiAlH_4$ (113 mg, 3 mmol) in dry ether (20 ml) maintained at RT. The mixture was left stirred for 2 hr, excess of reagent decomposed by cautious addition of cold water, extracted with ether, washed with brine, dried ($MgSO_4$), solvents

evaporated and the residue chromatographed on silica gel. Elution with benzene:ethyl acetate::90:10 gave 240 mg (92.3%) of the diene alcohol, bp 102°/0.1 torr, as a mixture of isomers. Isomerization to (E,E) 8,10-dodecadien 1-ol was done by leaving a solution of the diene in dry hexane (5 ml) containing iodine (0.5g), in direct sunlight, for 5-6 days. Solvents were evaporated and the residue chromatographed on silica gel. Elution with benzene:ethyl acetate::90:10 gave pure (E,E) isomer with no loss in yields.

Anal. Calcd. for $C_{12}H_{22}O$ (Mol. Wt. 182)
C, 79.12; H, 12.09%
Found C, 79.34; H, 11.89%

ir : ν_{max}(neat) (cm^{-1}): 3350 (hydroxyl), 1655, 970 (double bond).

nmr: $\delta_{(CDCl_3)}$: (270 MHz) 1.7 (dd, $C\underline{H}_3$-CH=CH-), 3.6(t,-$C\underline{H}_2$-OH), 5.35(dt,-CH=C$\underline{H}$-CH_2), 5.6(m, CH_3-C$\underline{H}$=CH-), 6.0(m, CH_3-CH=C$\underline{H}$-), 6.32(dd,-CH=CH-C$\underline{H}$=CH-CH_2-)

XIV. Preparation of methyl 10-undecynoate (23)

a. 10,11-Dibromo methyl undecanoate (21)

To a paddle stirred and an ice-cooled solution of methyl 10-undecenoate (2) (50g, 0.25 mol) in CCl_4 (150 ml) was added bromine (40.5g, 0.25 mol), in drops. The mixture was then allowed

to attain RT, solvents distilled off, the crude dibromo ester transferred to a china dish and rigorously dried *in vacuo*, yield 90.3g (100%). This sample of 21 was used as such for the following experiment.

b. Dehydrobromination of 21: Isolation of 10-undecynoic acid (22)

A very efficiently paddle-stirred mixture of the dibromo compound 21 (90.3g, 0.25 mol) and aqueous KOH (150g KOH in 90 ml H_2O) was held at 150-160°C for 8 hr. The tendency for frothing was curbed with periodical addition of small amounts of sodium lauryl sulphate. The reaction mixture was cooled, diluted with water (500 ml), acidified with cold 6N H_2SO_4, extracted with ether repeatedly, washed with brine, dried ($MgSO_4$) and solvents evaporated. The residue on distillation gave 24.42g (53.1%) of 22; bp 124°/3 torr.

Anal. calcd. for $C_{11}H_{18}O_2$ (Mol. Wt. 182)
C, 72.53; H, 9 .89%
Found C, 72.78; H, 10.12%

ir : ν_{max}(neat)(cm^{-1}): 3310 (C-H), 2110 (-C≡C-), 1710(acid).

nmr: $\delta_{(CCl_4)}$: 1.71 (t, 1H, -C≡C-H), 1.9-2.5 (m, 4H, -CH_2-C≡C-H, -CH_2-COOH), 11.2 (s, 1H, -COOH).

c. Fischer esterification of 10-undecynoic acid (22): Preparation of methyl 10-undecynoate (23)

A stirred mixture of 10-undecynoic acid (21g, 0.12 mol), dry methanol(500 ml) and conc. H_2SO_4 (0.5 g) was refluxed for 4 hr , solvents evaporated, the residue cautiously added to ice-cold water (500 ml), the upper oily layer extracted with ether (3 x 150 ml), washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to yield 22 g (99%) of 23, bp 77-80°/0.4 torr.

Anal. Calcd. for $C_{12}H_{20}O_2$ (Mol. Wt. 196)
C, 73.42; H, 10.2 %
Found C, 73.50; H, 9.93%

ir : ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2110 (-C≡C-) 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 1.71 (t, 1H, -C≡C-H), 1.9-2.4 (m, 4H, -CH_2-C≡C-, -CH_2-COOMe), 3.54 (s, 3H, -COOCH_3).

XV. Preparation of key synthon, 1-tetrahydropyranyloxy 10- undecyne (25)

a. Lithium aluminium hydride reduction of methyl 10-undecynoate (23): Isolation of 10-undecynol (24)

A solution of 23 (5.883, 0.03 mol) in dry ether (15 ml) was added to a well stirred suspension of $LiAlH_4$ (0.768g,0.02 mol) in dry ether (20 ml) maintained at RT. The mixture was left

stirred for 4 hr , excess reagent decomposed cautiously with water, extracted with ether, washed with brine, dried ($MgSO_4$) and evaporated to yield 4.932g (97.8%) of 10-undecyn 1-ol (24).

Anal. Calcd. for $C_{11}H_{20}O$ (Mol. Wt. 168)
C, 78.57; H, 11.9 %
Found C, 78.99; H, 11.83%

ir : ν_{max}(neat) (cm^{-1}): 3350 (hydroxyl), 3310 (-C≡C-H), 2110 (-C≡C-).

nmr: δ (CCl_4): 1.8 (t, 1H, -C≡C-H), 1.9-2.3 (m, 2H, -CH_2-C≡C-), 3.55(t, 2H, -CH_2-OH), 3.6 (s, 1H, -OH).

b. Preparation of pyridinium p-toluenesulfonate (PPTS)

To stirred pyridine (12.1 ml, 150 mmol) at RT was added p-toluene sulfonic acid monohydrate (5.7g, 30 mmol). The reaction mixture was left stirred for 0.33 hr., excess pyridine evaporated at 60° in vacuo. The residue on crystallization from acetone gave 6.8g (90%) of PPTS, mp 119° (lit.[59] mp 120°).

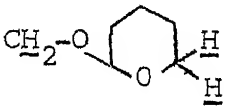
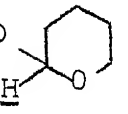
c. Preparation of 1-tetrahydropyranyloxy 10-undecyne (25)

A mixture of 10-undecynol (24) (5.042g, 0.03 mol), 5,6-dihydropyran (3.784g, 0.045 mol), dry dichloromethane (150 ml) and PPTS (0.783g, 0.003 mol) was left stirred for 4 hr at RT, diluted with ether (150 ml), washed with half-satd. brine, dried ($MgSO_4$), solvents evaporated and the residue on distillation

gave 7.22g (95.6%) of 25, bp 88-90°/0.2 torr.

Anal. Calcd. for $C_{16}H_{28}O_2$ (Mol. Wt. 252)
C, 76.19; H, 11.11%
Found C, 76.69; H, 10.89%

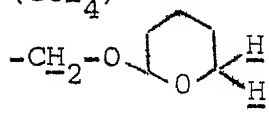
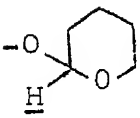
ir : ν_{max}(neat)(cm^{-1}): 3310 (C≡C-H), 2110 (-C≡C-), 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 1.7 (t, 1H, -C≡C-H), 1.85-2.3 (m, 2H, $-CH_2-C\equiv C-$), 3.0-4.0 (m, 4H, $-CH_2-O$ ), 4.45 (s, 1H, O ).

XVI. Demonstration of acetylide formation: Preparation of 11-deutero 1-tetrahydropyranyloxy 10-undecyne

A solution of butyl lithium (0.128g, 0.002 mol) in hexane (1 ml) was added, in drops, to a stirred solution of 1-tetrahydropyranyloxy 10-undecyne (25) (0.252g, 0.001 mol) in dry THF (15 ml), maintained below 10°. Deuterium oxide (1 ml) was then added, in drops, keeping the reaction mixture below 25°, extracted with hexane (2 x 100 ml), washed with water, brine, dried ($MgSO_4$), solvents evaporated to give 0.255g (~ 100%) of 25 which contained at least 98% deuterium at the 11 position (IR, NMR).
bp 85-87°/0.05 torr.

ir: ν_{max}(neat)(cm^{-1}): 2590 (-C-D), 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 2.03 (t, 2H, $-C\equiv C-\underline{CH_2}-$), 3.0-4.0 (m, 4H, ), 4.45 (s, 1H, ).

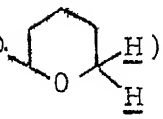
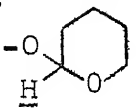
XVII. Synthesis of (Z) 10-tetradecenol (28): Pheromone of Archips semiferanus

a. Alkylation of 1-tetrahydropyranyloxy 10-undecyne (25): Preparation of 1-tetrahydropyranyloxy 10-tetradecyne(26)

A solution of butyl lithium (1.28g, 0.02 mol) in hexane (8.5 ml) was added to a stirred and cooled ($< 10^{\circ}$) solution of 1-tetrahydropyranyloxy 10-undecyne (25) (2.52g, 0.01 mol) in dry THF (15 ml). A solution of n-propyl bromide (2.26g, 0.02 mol) in dry HMPA (20 ml) was then added, in drops maintaining the temperature $< 25^{\circ}$. The reaction mixture was left stirred for 0.5 hr, poured on to ice-water, extracted with hexane (3 x 100ml), washed with water, brine, dried ($MgSO_4$), solvents evaporated and the residue distilled to give 2.76g (93.8%) of 26, bp $118-120^{\circ}/0.05$ torr.

Anal. Calcd. for $C_{19}H_{34}O_2$ (Mol. Wt. 294)
C, 77.55; H, 11.56%
Found C, 77.34; H, 12.0 %

ir : ν_{max}(neat) (cm^{-1}): 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 870(m), 815(m).

nmr: δ (CCl_4): 0.9 (t, 3H, $-CH_3$), 1.85-2.2 (m, 4H, $-CH_2-C\equiv C-CH_2-$), 3.0-4.0 (m, 4H, ), 4.4 (s, 1H, ).

b. De-protection of 1-tetrahydropyranyloxy 10-tetradecyne(26): Preparation of 10-tetradecynol (27)

A mixture of 26 (2.357g, 0.008 mol), ethanol (15 ml) and PPTS (0.196g, 0.0008 mol) was left stirred for 4 hr at 70°, solvents evaporated *in vacuo* and the residue admixed with ether (200 ml), washed with brine, dried ($MgSO_4$) and evaporated to yield 1.789g of the crude 27, which was distilled, bp 90-95°/0.05 torr; yield 1.54g (92%).

Anal. Calcd. for $C_{14}H_{26}O$ (Mol. Wt. 210)
C, 80.0 ; H, 12.38%
Found C, 79.71; H, 12.33%

ir : ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl).

nmr: δ (CCl_4): 0.9 (t, 3H, $-CH_3$), 1.85-2.2 (m, 4H, $-CH_2-C\equiv C-CH_2$), 3.4 (t, 2H, $-CH_2-OH$), 3.72 (s,1H,-OH).

c. Stereoselective hydrogenation of 10-tetradecynol (27): Preparation of (Z) 10-tetradecenol (28)

A stirred solution of 10-tetradecynol (27) (0.212g, 0.001 mol) in methanol (5 ml) was partially hydrogenated over

5% $Pd/BaSO_4$ (0.04g), further de-activated with a micro drop of synthetic quinoline. The hydrogen uptake was monitored and the reaction stopped soon after the calculated volume was absorbed. The catalyst was filtered off, solvents evaporated and the residue chromatographed over a short column of silica gel. Elution with benzene:ethyl acetate::90:10 gave 0.207g (96.7%) of 28.

Anal. Calcd. for $C_{14}H_{28}O$ (Mol. Wt. 212)
C, 79.24; H, 13.20%
Found C, 79.34; H, 13.45%

ir : ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.85 (t, 3H, $-CH_3$), 1.75-2.15 (m, 4H, $-CH_2-C\equiv C-CH_2-$), 3.5 (t, 2H, $-CH_2OH$), 3.6 (s, 1H, $-OH$), 5.05-5.35 (m, 2H, $-CH=CH-$).

XVIII. Synthesis of the Spodoptera frugiperda pheromone homolog 31

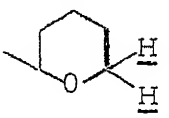
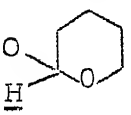
a. Alkylation of 1-tetrahydropyranyloxy 10-undecyne (25): Preparation of 1-tetrahydropyranyloxy 10-pentadecyne(29)

A solution of butyl lithium (1.28g, 0.02 mol) in hexane (8.5 ml) was added to a stirred and cooled ($< 10^{\circ}$) solution of 25 (2.52g, 0.01 mol) in dry THF (15 ml). A solution of n-butyl bromide (2.74g, 0.02 mol) in HMPA (20 ml) was then added, in drops, keeping the temperature $< 25^{\circ}$. After 0.5 hr the reaction mixture was poured on to ice-water, extracted with hexane

(3 x 100 ml), washed with water, brine, dried ($MgSO_4$), solvents evaporated and the residue distilled to give 2.94g (95.6%) of 29, bp 125-7°/0.02 torr.

Anal. Calcd. for $C_{20}H_{36}O_2$ (Mol. Wt. 308)
C, 77.92; H, 11.68%
Found C, 77.53; H, 11.97%

ir : ν_{max}(neat)(cm^{-1}): 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 0.85 (t, 3H, $-CH_3$), 1.85-2.2 (m, 4H, $-CH_2-C\equiv C-CH_2-$), 3.0-4.0 (m, 4H, $-CH_2-O$ ), 4.4 (s, 1H, ).

b. Direct transformation of 1-tetrahydropyranyloxy 10-pentadecyne 29 to 1-acetoxy 10-pentadecyne (30)

A solution of 29 (2.61g, 0.0085 mol) in AcOH:AcCl::10:1 (10 ml) was left aside overnight, poured on to crushed ice, extracted with hexane (3 x 100 ml), washed with 10% $NaHCO_3$, brine, dried ($MgSO_4$), solvents evaporated and the residue distilled to give 2.017g (88%) of 30, bp 81-82°/0.02 torr.

Anal. Calcd. for $C_{17}H_{30}O_2$ (Mol. Wt. 266)
C, 76.69; H, 11.27
Found C, 76.23; H, 10.92%

ir: ν_{max}(neat)(cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.85 (t, 3H, $-C\underline{H}_3$), 1.85-2.2 (m, 7H, $-OCOC\underline{H}_3$, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 3.9 (t, 2H, $-C\underline{H}_2-OCOCH_3$).

c. Stereoselective hydrogenation of 1-acetoxy 10-pentadecyne (30): Preparation of 1-acetoxy (Z) 10-pentadecene (31)

A stirred solution of 30 (0.266g, 0.001 mol) in methanol (5 ml) was hydrogenated over 5% $Pd/BaSO_4$ which was further deactivated with a micro-drop of synthetic quinoline. Hydrogen uptake was monitored and the reaction was stopped soon after the calculated volume was absorbed. The catalyst was filtered, solvents evaporated and the residue chromatographed on silica gel. Elution with benzene gave 0.266g (99%) of 31.

Anal. Calcd. for $C_{17}H_{32}O_2$ (Mol. Wt. 268)
C, 76.11; H, 11.94%
Found C, 75.93; H, 12.1~%

ir : ν_{max}(neat) (cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.85 (t, 3H, $-C\underline{H}_3$), 1.85-2.2 (m, 7H, $-OCOC\underline{H}_3$, $-C\underline{H}_2-C=C-C\underline{H}_2-$), 3.9 (t, 2H, $-C\underline{H}_2OCOCH_3$), 5.08-5.35 (m, 2H, olefinic).

XIX. Preparation of methyl 9-decynoate (34)

a. Addition of bromine to 9-decenoic acid (10): Preparation of 9,10-dibromo decanoic acid (32)

To a well stirred and ice-cooled solution of

9-decenoic acid (10) (17.0g, 0.1 mol) in carbon tetrachloride (50 ml) was added, in drops, bromine (16g, 0.1 mol). The reaction mixture was allowed to attain RT, solvents evaporated, the residue transferred to a china dish, thoroughly dried *in vacuo* and used as such for the following experiment; yield 33g (100%).

b. Dehydrobromination of 32: Isolation of 10-decynoic acid(33)

A very efficiently paddle-stirred mixture of 32 and aqueous KOH (45g KOH in 27 ml H_2O) was held at 150-160° for 8 hr. The tendency for frothing was curbed by periodical addition of small amounts of sodium lauryl sulphate. Work-up as described in Experiment XIV.b, for the related 21 ⟶ 22 change, gave 17g of crude product which on distillation gave 13g (78%) of 9-decynoic acid (33), bp 85-90°/0.05 torr.

Anal. Calcd. for $C_{10}H_{16}O_2$ (Mol. Wt. 168)
C, 71.4 ; H, 9.5 %
Found C, 71.42; H, 9.40%

ir : ν_{max}(neat)(cm^{-1}): 3300 (-C≡C-H), 2110 (-C≡C-), 1710 (acid).

nmr: $\delta_{(CCl_4)}$: 1.94 (t, 1H, H-C≡C-), 2.05-2.51 (m, 4H, -C≡C-CH_2, -CH_2-COOH), 12.01 (br, 1H, -COOH).

c. Fischer esterification of 9-decynoic acid (33): Preparation of methyl 9-decynoate (34)

A stirred mixture of 9-decynoic acid (33), dry methanol (500 ml) and conc. H_2SO_4 (0.5g) was refluxed for 2 hr. Work-up as described in Experiment XIV.c, for the related 22 ⟶ 23 change gave 23g (100%) of methyl 9-decynoate; bp 79-80°/0.05 torr.

Anal. Calcd. for $C_{11}H_{18}O_2$ (Mol. Wt. 182)
C, 72.53; H, 9.89%
Found C, 72.35; H, 9.56%

ir : ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2110 (-C≡C-), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 1.85 (t, 1H, H-C≡C-), 2.05-2.4 (m, 4H, -C≡C-CH_2, -CH_2-$COOCH_3$), 3.65 (s, 3H, -$COOCH_3$).

XX. Preparation of key synthon, 1-tetrahydropyranyloxy 9-decyne (36)

a. $LiAlH_4$ reduction of methyl 9-decynoate (34): Isolation of 10-decynol (35)

A solution of 34 (5068g, 0.028 mol), in dry ether (10 ml), was added to a well stirred suspension of $LiAlH_4$ (0.684g, 0.018 mol) in dry ether (20 ml) maintained at RT. The mixture left stirred for 4 hr and work-up as described in Experiment XV.a for the

related 23 ⟶ 24 change gave 3.5g (83%) 35, bp 74-75°/0.04 torr.

Anal. Calcd. for $C_{10}H_{18}O$ (Mol. Wt. 154)
C, 77.9; H, 11.68%
Found C, 77.55;H, 11.68%

ir : ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl), 3310 (-C≡C-H), 2110 (-C≡C-).

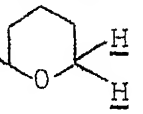
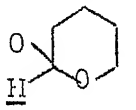
nmr: $\delta_{(CCl_4)}$: 1.81 (t, 1H, -C≡C-H), 1.95-2.3 (m, 2H, -C≡C-CH_2-), 3.55(t, 2H, -CH_2-OH), 3.6 (s, 1H, -OH).

b. Protection of alcohol 35: Preparation of 1-tetrahydropyranyloxy 9-decyne (36)

A mixture of 9-decynol (35) (6.16g, 0.04 mol), 5,6-dihydropyran (5.04g, 0.06 mol), dry dichloromethane (200 ml) and PPTS (1.0g, 0.004 mol) was left stirred for 4 hr at RT. Work-up as described in Experiment XV.c for the related 24 ⟶ 25 change gave 9.32g (98%) of 36, bp 108-110°/0.05 torr.

Anal. Calcd. for $C_{15}H_{26}O_2$ (Mol. Wt. 238)
C, 75.62; H, 10.92%
Found C, 75.77; H, 11.07%

ir : ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2110 (-C≡C-), 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 1.85 (t, 1H, -C≡C-H), 2.0-2.5 (m, 2H, -C≡C-CH_2-), 3.0-4.0 (m, 4H, -CH_2-O ), 4.5 (s, 1H, ).

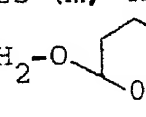
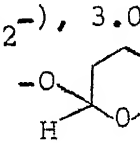
XXI. Synthesis of 1-acetoxy (Z) 9-tetradecene: The pheromone of Spodopetra frugiperda (39)

a. Alkylation of 1-tetrahydropyranyloxy 9-decyne (36): Preparation of 1-tetrahydropyranyloxy 9-tetradecyne (37)

A solution of butyl lithium (1.28g, 0.02 mol) in hexane (8.5 ml) was added to a stirred and cooled (<10°) solution of 36 (2.38g, 0.01 mol) in dry THF (15 ml). A solution of n-butyl-bromide (2.74g, 0.02 mol) in HMPA (20 ml) was then added, in drops, keeping the temperature below 25°, work-up as described in Experiment XVIII.a for the related 25 ⟶ 29 change gave 2.8g (96%) of 37, bp 128-130°/0.03 torr.

Anal. Calcd. for $C_{19}H_{34}O_2$ (Mol. Wt. 294)
C, 77.55; H, 11.56%
Found C, 77.35; H, 11.34%

ir : ν_{max}(neat) (cm^{-1}): 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, -CH_3), 2.0-2.25 (m, 4H, -CH_2-C≡C-CH_2-), 3.0-4.0 (m, 4H, -CH_2-O ), 4.5 (s, 1H, ).

b. Direct transformation of 1-tetrahydropyranyloxy 9-tetradecyne (37) to 1-acetoxy 9-tetradecyne (38)

A solution of 37 (2.38g, 0.008 mol) in AcOH:AcCl::10:1 (10 ml) was left aside overnight. Work-up as described in Experiment XVIII.b for the related 29 $\longrightarrow$ 30 change gave 1.79g (89%) of 38, bp 70-75°/0.05 torr.

Anal. Calcd. for $C_{16}H_{28}O_2$ (Mol. Wt. 252)
C, 76.19; H, 11.11%
Found C, 75.86; H, 11.07%

ir : ν_{max}(neat)(cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $-CH_3$), 1.98 (s, 3H, $-OCOCH_3$), 2.0-2.25 (m, 4H, $-CH_2-C\equiv C-CH_2$), 3.95 (t, 2H, $-CH_2-OCOCH_3$).

c. Stereoselective hydrogenation of 1-acetoxy 9-tetradecyne(38): Preparation of 1-acetoxy (Z) 9-tetradecene (39)

A stirred solution of 38 (0.252g, 0.01 mol) in methanol (5 ml) was hydrogenated over 5% $Pd/BaSO_4$ catalyst (0.04g) which was further deactivated with a micro-drop of synthetic quinoline. Hydrogen uptake was monitored and the reaction was stopped soon after the calculated amount was absorbed. The catalyst was filtered, solvents evaporated and the residue chromatographed over silica gel. Elution with benzene gave 0.25g (99%) of 39, bp 110-115°/0.05 torr.

Anal. Calcd. for $C_{16}H_{30}O_2$ (Mol. Wt. 254)

C, 75.59; H, 11.81%

Found C, 75.66; H, 11.56%

ir : ν_{max}(neat)(cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-C\underline{H}_3$), 1.8-2.25 (br, 7H, $-OCOC\underline{H}_3$, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 3.95 (t, 2H, $-C\underline{H}_2-OAc$) 5.32 (m, 2H, olefinic).

XXII. Synthesis of 1-acetoxy (Z) 9-dodecene (42): The pheromone of Paralobesia viteana

a. Alkylation of 1-tetrahydropyranyloxy 9-decyne (36)
Preparation of 1-tetrahydropyranyloxy 9-dedecyne(40)

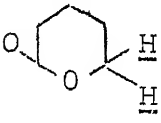
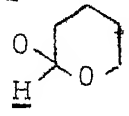
A solution of butyl lithium (1.28g, 0.02 mol) in hexane (8.5 ml) was added to a stirred and cooled ($< 10^{\circ}$) solution of 36 (2.38g, 0.01 mol) in dry THF (15 ml). A solution of ethyl bromide (2.18g, 0.02 mol) in HMPA (20 ml) was then added keeping the temperature $< 25^{\circ}$. Work-up as described in Experiment XVIII.a for the related 25 $\longrightarrow$ 29 change gave 2.6g (97.7%) of 40, bp 92-93°/0.05 torr.

Anal. Calcd. for $C_{17}H_{30}O_2$ (Mol. Wt. 266)

C, 76.69; H, 11.27%

Found C, 76.68; H, 11.40%

ir : ν_{max}(neat) (cm^{-1}): 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m).

nmr: $\delta_{(CCl_4)}$: 1.1 (t, 3H, $-CH_3$), 1.95-2.25 (m, 4H, $-CH_2-C\equiv C-CH_2$), 3.0-4.0 (m, 4H, $-CH_2-O$ ), 4.5 (s, 1H, ).

b. Direct transformation of 1-tetrahydropyranyloxy 9-dodecyne (40) to 1-acetoxy 9-dodecyne (41)

A solution of 40 (2.391g, 0.0089 mol) in AcOH:AcCl::10:1 (10 ml) was left aside overnight. Work-up as described in Experiment XVIII.b for the related 29 ⟶ 30 change gave 1.98g (94%) of 41, bp 75-80°/0.05 torr.

Anal. Calcd. for $C_{14}H_{24}O_2$ (Mol. Wt. 224)
C, 75.0; H, 10.7%

Found C, 75.0; H, 11.0%

ir : ν_{max}(neat) (cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 1.1 (t, 3H, $-CH_3$), 1.95 (s, 3H, $-OCOCH_3$), 2.0-2.25 (m, 4H, $-CH_2-C\equiv C-CH_2-$), 4.0 (t, 2H, $-CH_2-OAc$).

c. Stereoselective hydrogenation of 1-acetoxy 9-dodecyne (41): Preparation of 1-acetoxy (Z) 9-dodecene (42)

A stirred solution of 41 (0.224g, 0.001 mol) in methanol (5 ml) was hydrogenated and worked up as described in Experiment XXI.c for the related 38 ⟶ 39 change. The crude product on

chromatography over silica gel and elution with benzene gave 0.223g (98.6%) of 42 .

Anal. Calcd. for $C_{14}H_{26}O_2$ (Mol. Wt. 226)

C, 74.3; H, 11.5 %

Found C, 74.3; H, 11.48%

ir : ν_{max}(neat) (cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $-C\underline{H}_3$), 1.9-2.25 (m, 7H, $-OCOC\underline{H}_3$, $-C\underline{H}_2-CH=CH-C\underline{H}_2$), 3.95 (t, 2H, $-C\underline{H}_2-OAc$), 5.3 (m, 2H, olefinic).

XXIII. Synthesis of 1-acetoxy (Z)(E) 9,12 tetradecadiene (45): The pheromone of Prodenia eridania (Prodenialure)

a. Alkylation of 1-tetrahydropyranyloxy 9-decyne (36) with crotyl bromide: Preparation of 1-tetrahydropyranyloxy(E) tetradeca 12-ene, 9-yne (43)

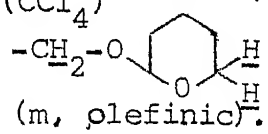
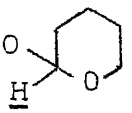
A solution of butyl lithium (1.28g, 0.02 mol) in hexane (8.5 ml) was added to a stirred and cooled (< 10°) solution of 36 (2.38g, 0.01 mol) in dry THF (15 ml). A solution of E-crotyl bromide (2.7g, 0.02 mol) in HMPA (20 ml) was then added, in drops, keeping the temperature below 25°. Work-up as described in Experiment XVIII.a for the related 25 ⟶ 29 change gave 2.86g (98%) of 43, bp 105°/0.05 torr.

Anal. Calcd. for $C_{16}H_{28}O_2$ (Mol. Wt. 252)

C, 78.08; H, 10.95%

Found C, 77.93; H, 10.82%

ir : ν_{max}(neat)(cm^{-1}): 1135(s), 1120(s), 1080(s), 1030(s), 980(m), 900(m), 870(m), 815(m), 970 (trans double bond).

nmr: $\delta_{(CCl_4)}$: 2.1(br, -CH=CH-CH_2-C≡C-), 3.1-4.0 (m, 4H, ), 4.6(s, 1H, ), 5.4-5.7 (m, olefinic).

b. Direct transformation of 1-tetrahydropyranyloxy (E) tetradeca 12-ene, 9-yne (43) to 1-acetoxy (E) tetradeca 12-ene, 9-yne (44)

A solution of 43 (2.239g, 0.08 mol) in AcOH:AcCl::10:1 (10 ml) was left aside overnight. Work-up as described in Experiment XVIII.b for the related 29 ⟶ 30 change gave 1.991g (99%) of 44, bp 105-107°/0.05 torr.

Anal. Calcd. for $C_{16}H_{26}O_2$ (Mol. Wt. 250)

C, 76.8 ; H, 10.4 %

Found C, 76.58; H, 10.16%

ir : ν_{max}(neat)(cm^{-1}): 1735 (acetate, 970 (trans double bond).

nmr: $\delta_{(CCl_4)}$: 1.75 (m, 3H, $-C\underline{H}_3$), 1.95-2.2 (m , 5H, $-OCOC\underline{H}_3$, $-HC{=}CH-C\underline{H}_2-C{\equiv}C-$), 4.01 (t, 2H, $-C\underline{H}_2-OAc$), 5.3-5.95 (m, 2H, olefinic).

c. Stereoselective hydrogenation of 1-acetoxy (E) tetradeca 12-ene, 9-yne (44): Preparation of 1-acetoxy (Z)(E) 9,12-tetradecadiene (45)

A stirred solution of 44 (0.25g, 0.001 mol) in methanol (5 ml) was hydrogenated and worked up as described in Experiment XXI.c for the related 38 ⟶ 39 change. The crude product on chromatography over silica gel and elution with benzene gave 0.248g (98%) of 45.

Anal. Calcd. for $C_{16}H_{28}O_2$ (Mol. Wt. 252)
C, 76.19; H, 11.11%
Found C, 75.88; H, 11.48%

ir : ν_{max}(neat)(cm^{-1}): 1735 (acetate), 970 (trans doublebond).

nmr: $\delta_{(CCl_4)}$: 1.6 (t, 3H, $-C\underline{H}_3$), 1.9 (s, 3H, $-OCOC\underline{H}_3$), 2.5-2.8 (m, 2H, $-HC{=}CH-C\underline{H}_2-CH{=}CH$), 3.9 (t, 2H, $-C\underline{H}_2-OAc$), 4.95-5.6 (br, 4H, olefinic).

silica gel and elution with benzene:ethyl acetate::85:15, gave 0.207g (98%) of 47, bp 85-87°/0.03 torr.

Anal. Calcd. for $C_{14}H_{28}O$ (Mol Wt. 212)
C, 79.24; H, 13.2 %
Found C, 79.49; H, 13.17%

ir : ν_{max}(neat) (cm^{-1}): 3350 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-C\underline{H}_3$), 1.8-2.25 (m, 4H, $-C\underline{H}_2CH=CH-C\underline{H}_2-$), 3.5 (t, 2H, $-C\underline{H}_2OH$), 3.7 (s, 1H, $-O\underline{H}$), 5.1-5.4 (m, 2H, olefinic).

c. Oxidation of (Z) 9-tetradecenol (47): Preparation of (Z) 9-tetradecenal (48)

Neat (Z) 9-tetradecenol (47) (0.633g, 0.03 mol) was added, in one lot, to a stirred suspension of pyridinium chlorochromate (1g, 0.0045 mol) in dry dichloromethane (5 ml). The reaction mixture was left stirred for 1.5 hr, admixed with dry ether (50 ml), decanted, the residue thoroughly extracted with dry ether (3 x 25 ml), the combined extracts passed through a sintered funnel packed with silica gel, solvents evaporated in vacuo and the residue on preparative tlc using benzene as developer gave 0.563g (89%) of 48.

Anal. Calcd. for $C_{14}H_{26}O$ (Mol. Wt. 210)
C, 80.0; H, 12.38%
Found C, 79.55;H, 11.9 %

ir : ν_{max}(neat) (cm^{-1}): 1730 (aldehyde).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $-C\underline{H}_3$), 1.85-2.2 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 2.34 (t, 2H, $-C\underline{H}_2-CHO$), 5.2-5.5 (m, 2H, olefinic), 9.7 (s, 1H, $-C\underline{H}O$).

XXV. Synthesis of ethyl tetradeca (Z) 9-enoate (51): The pheromone of Bombus lucorum

a. Alkylation of 9-decynoic acid (33): Preparation of 9-tetradecynoic acid (49)

A solution of butyl lithium (1.92g, 0.03 mol) in hexane (12.5 ml) was added to a stirred solution of 9-decynoic acid (33) (1.684g, 0.01 mol) in HMPA (30 ml) maintaining the temperature $\sim 0^{\circ}$. Neat butyl bromide (4.13g, 0.03 mol) was then added, in drops, keeping the temperature $\sim 0^{\circ}$. The reaction mixture was left stirred overnight at RT, poured on to ice water, acidified with cold 2N H_2SO_4, extracted with ether, washed with brine, dried ($MgSO_4$), solvents evaporated and the resulting crude 49 (2.5g, 100%) was used as such in the following experiment.

ir: ν_{max}(neat) (cm^{-1}): 1700 (acid).

b. Fischer esterification of 9-tetradecynoic acid (49): Preparation of ethyl 9-tetradecynoate (50)

A mixture of 49 (2.5g, 0.011 mol), dry ethanol (75 ml), conc. H_2SO_4 (0.5g) was refluxed for 2hr, solvents evaporated,

the residue poured on to ice water (150 ml), extracted with ether (2 x 100 ml), washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$), solvents evaporated and the residue on distillation gave 2.0g (78%) of 50, bp 94-95°/0.05 torr.

Anal. Calcd. for $C_{16}H_{28}O_2$ (Mol. Wt. 252)
C, 76.19; H, 11.11%
Found C, 76.38; H, 10.89%

ir : ν_{max}(neat) (cm^{-1}): 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-CH_3$), 1.2 (t, 3H, $-OCOCH_2CH_3$), 2.0-2.4 (m, 6H, $-CH_2COOC_2H_5$, $-CH_2-C\equiv C-CH_2$), 4.05 (q, 2H, $-OCOCH_2CH_3$).

c. Stereoselective hydrogenation of ethyl 9-tetradecynoate(50): Preparation of ethyl tetradeca (Z) 9-enoate (51)

A stirred solution of 50 (0.252g, 0.001 mol) in ethanol (5 ml) was hydrogenated over 5% $Pd/BaSO_4$ (0.04g) which was further de-activated by addition of a micro drop of synthetic quinoline. Hydrogen uptake was monitored and the reaction was stopped after the calculated amount was absorbed. The catalyst was filtered, solvents evaporated and the residue chromatographed over silica gel. Elution with benzene gave 0.251g (98.4%) of 51.

Anal. Calcd. for $C_{16}H_{30}O_2$ (Mol. Wt. 254)

C, 75.59; H, 11.81%

Found C, 75.41; H, 11.67%

ir : ν_{max}(neat) (cm^{-1}): 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $-C\underline{H}_3$), 1.21 (t, 3H, $-COOCH_2C\underline{H}_3$), 1.85-2.35 (m, 6H, $-C\underline{H}_2COOC_2H_5$, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 4.05 (q, 2H, $-COOC\underline{H}_2CH_3$), 5.2-5.45 (m, 2H, olefinic).

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CHAPTER II

STUDY OF THE THERMAL TRANSFORMATION OF CASTOR OIL

II.A. INTRODUCTION

Practically every one of the very many synthons that arise from castor oil and which enjoy wide applicability in diverse facets relating to the use of carbon compounds in current civilization, owe their genesis to the rupture of the C_{18} castor oil backbone brought about thermally. The grouping that is responsible for this is the homoallyl alcohol ($-CH=CH-CH_2-\overset{OH}{\underset{|}{C}}H-$) unit. This moiety is placed medially in between the hydrophilic head and the hydrophobic tail.

The thermal rupture of castor oil to undecenoic acid and heptaldehyde was first discovered in 1827 and that in the presence of alkali to sebacic acid and 2-octanol in 1851.

Initially, these processes were examined, in view of their industrial importance, in an empirical manner chiefly to optimize yields and it was not until towards the present

mid-century that endeavours were initiated to understand them in terms of bond rupture and bond formation.

It was felt that an insight relating to the thermal rupture of castor oil under neutral and basic environments would enable the enhancement of the versatility of this abundantly available natural product as a source for useful synthons.

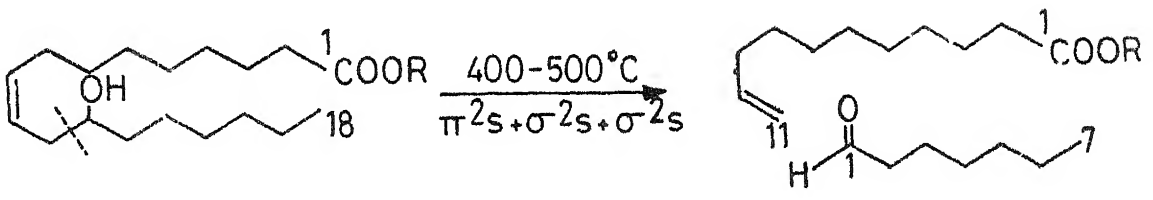
Results thus far available coupled with that from the present studies (SECTION II.C) decisively show that the thermal rupture of castor oil, under neutral conditions, to undecenoic acid and heptaldehyde proceeds <u>via</u> a $\pi^2s + \sigma^2s + \sigma^2s$ process which is more popularly known as a retro-ene reaction. In contrast, thermolysis under basic environments is complex, with the course of the reaction sensitive to a variety of factors, since the overall process involves a delightful milieu of hydride transfer, π migration, reverse Michael, reverse aldol, Meerwein-Ponndorf-Verley reduction and Cannizzaro reaction ! The outcome from the present investigation concerning these two processes is presented in CHART II.A.1.

Surprisingly, a careful survey revealed, that, unlike other functional groupings, the homoallyl alcohol moiety is not at all recognized as an important structural unit that is capable of unusual transformations and hardly finds mention as such in literature. It was felt that this lacuna deserves correction

CHART II A 1

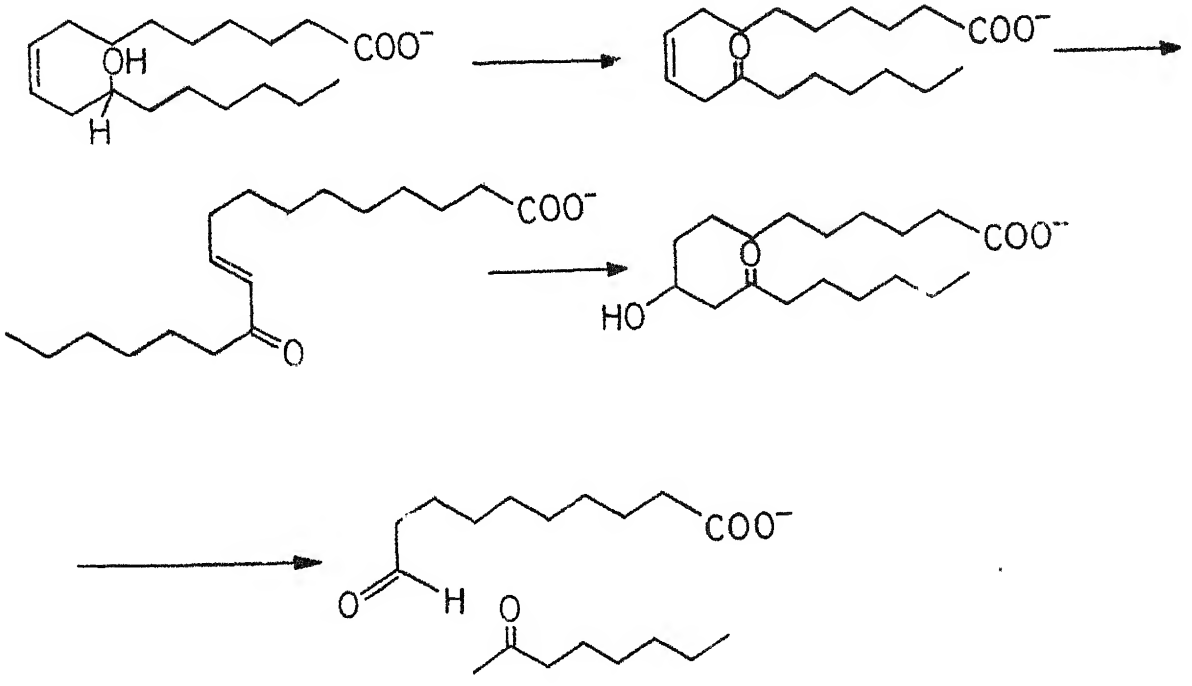
Thermal transformations of castor oil

a. under neutral conditions

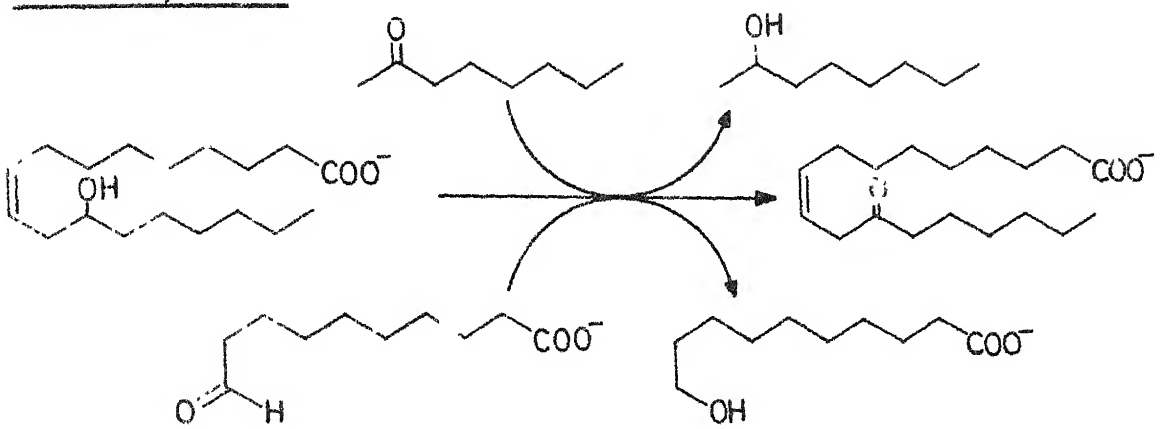


b. under "basic" environments

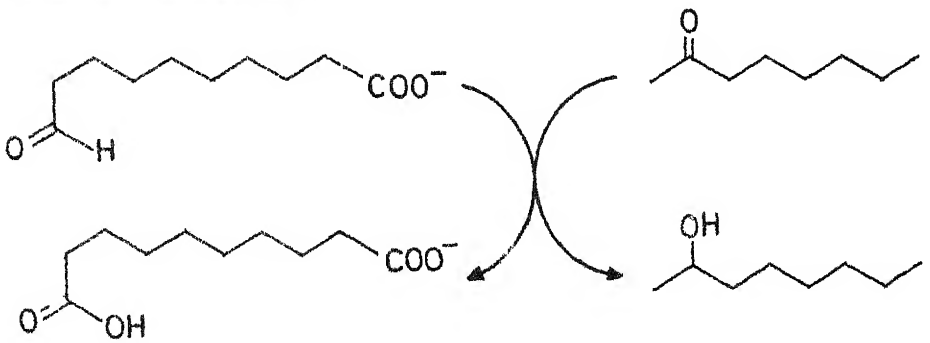
Primary reaction



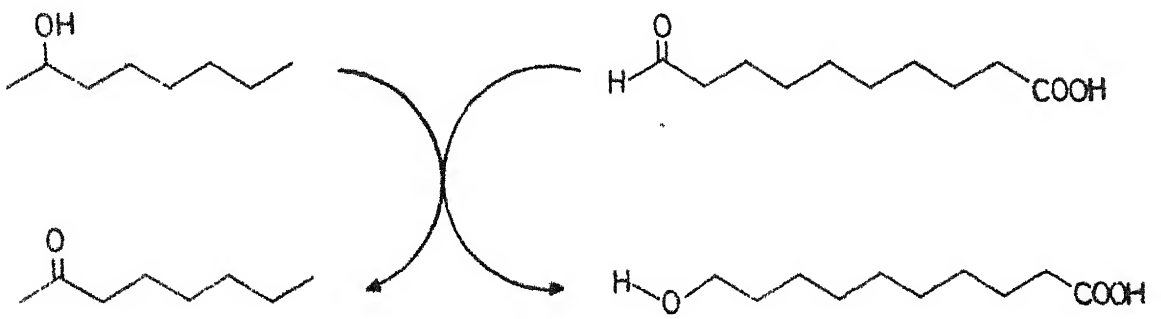
Redox system I



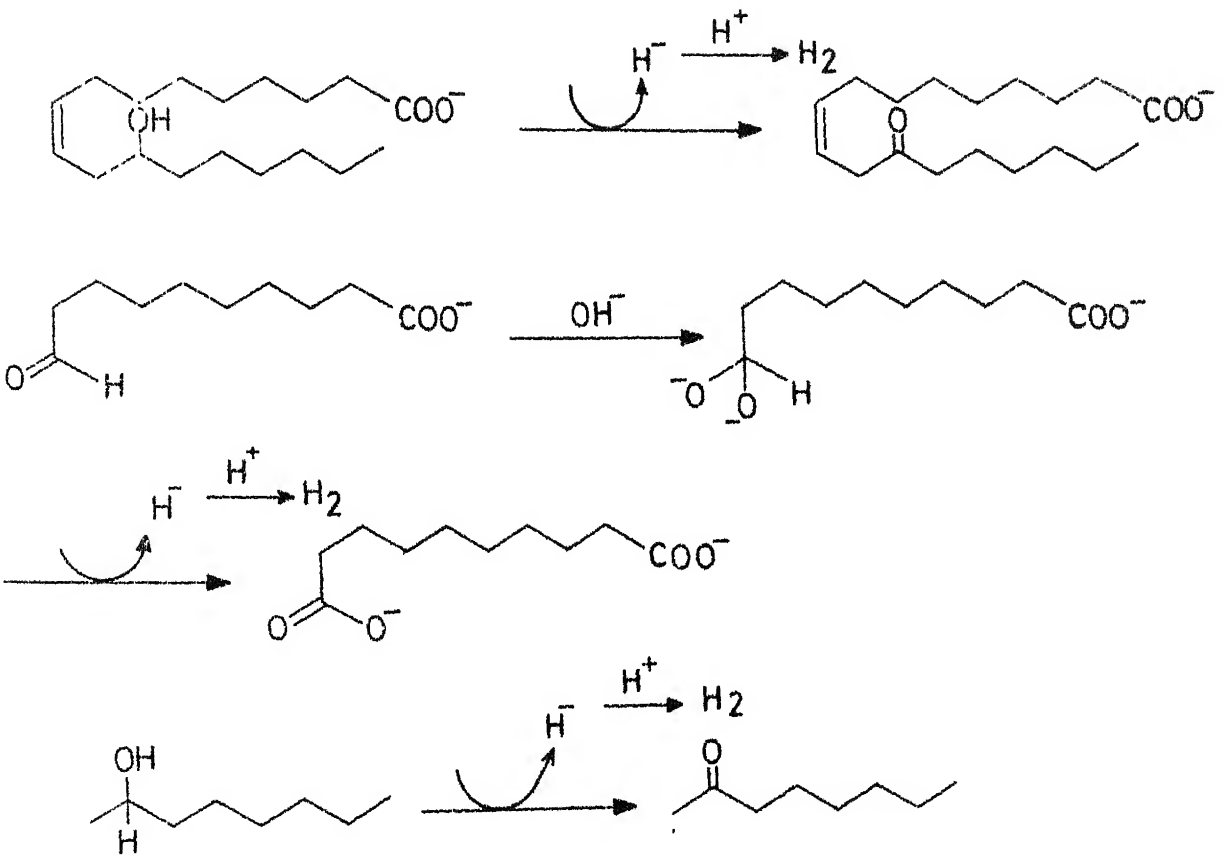
Redox system II



Redox system III



Uncoupled oxidations



and that the thermal reactions of this unit which comprise SECTION II.B would provide an appropriate background to the present work (II.C).

II.B. BACKGROUND

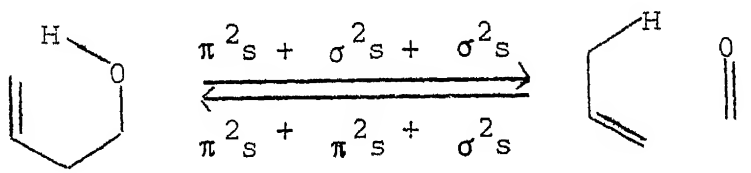
Thermolysis of homoallylic alcohols

As stated in SECTION II.A, the homoallyl alcohol unit is hardly recognized as such in literature. Indeed, there is even no uniformity in naming this system. The relevant moiety $(-CH=CH-CH_2-\underset{OH}{CH}-)$ is referred to as homoallyl alcohol or β,γ-unsaturated alcohol or γ,δ-unsaturated alcohol. The latter definition seems to be most appropriate.

The focus of the present discussion is the thermal fragmentation of the γ,δ-unsaturated alcohol unit under diverse reaction conditions. Consequently trivial reactions such as oxidation, dehydration as well as the rare transformation to saturated ketone under forcing conditions is not covered.

Thermal fragmentation of γ,δ-unsaturated alcohols

The smooth thermal transformation of γ,δ-unsaturated alcohols to carbonyl compounds is the reverse of ene reaction !

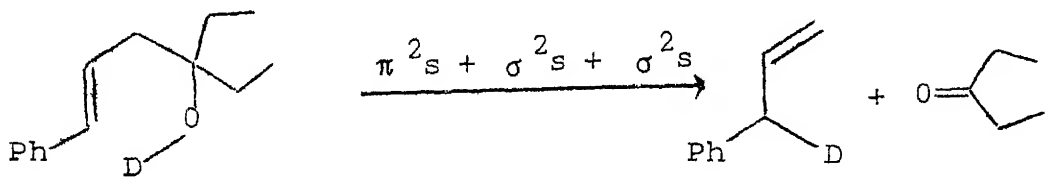


The reverse ene reaction is very well known.

The γ,δ-unsaturated alcohol system came under scrutiny because of interest in the thermal castor oil fragmentation.

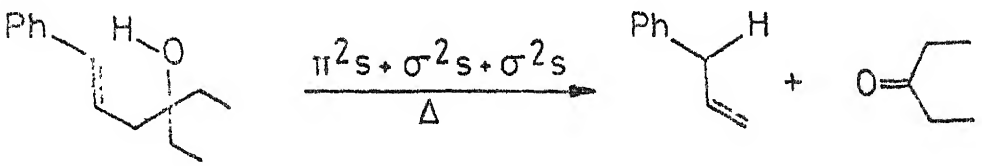
Barbot[1] with commendable intuition proposed in 1935 that the thermal transformation of castor oil to undecenoic acid and heptaldehyde proceeds by a six membered transition state, much as we understand to-day. A quarter century later Arnold and his group by a series of brilliant experiments, not only established the course of the transformation but also illustrated how this general reaction could be of synthetic utility.

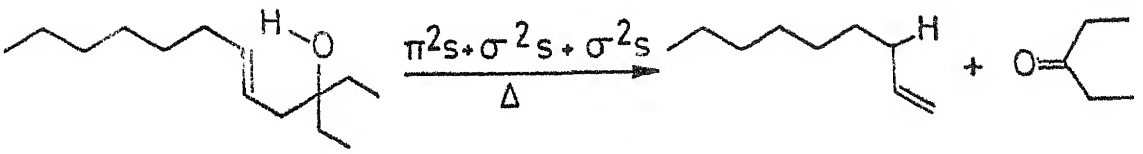
Thus, a variety of model γ,δ-unsaturated alcohols were demonstrated to undergo thermal rupture, as takes place in the case of castor oil (CHART II.B.1).[2] As anticipated the reaction is unimolecular and for the substrate $Ph\text{-}CH\overset{E}{=}CH\text{-}CH_2\text{-}C(C_2H_5)_2\text{-}OH$, the energy and entropy of activation has been found to be, 41.75 k.cal.mol^{-1} and -4.92 e.u at 600^{o}K.[3] The observed stereospecific deuterium transfer,

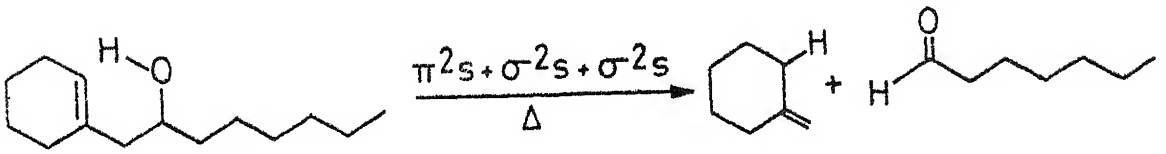


as well as the clean formation of the phenyl de-conjugated system strongly support a concerted cyclic transition state for the fragmentation of γ,δ-unsaturated alcohols.[4]

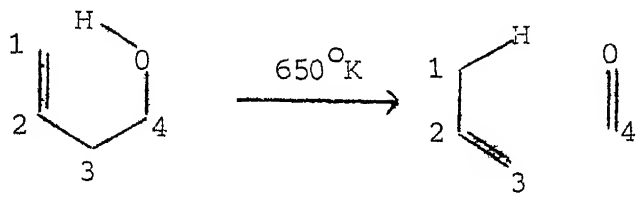
CHART II. B. 1


Ph
H
O
$\pi^2s + \sigma^2s + \sigma^2s$
Δ
Ph
H
+
O


H
O
$\pi^2s + \sigma^2s + \sigma^2s$
Δ
H
+
O


H
O
$\pi^2s + \sigma^2s + \sigma^2s$
Δ
H
+
O
H

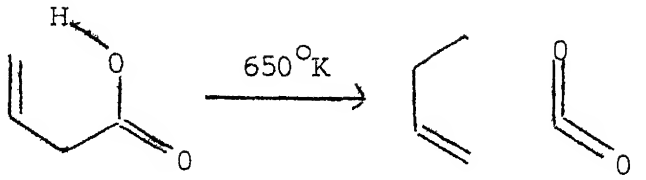
A study of the fragmentation of substituted but 1-ene 4-ols at 650°K enables the assessment of factors that influence the transition state.



Substitution	$10^3 k$
NIL	2.51
4 Me	7.37
4,4-Dimethyl	13.6
2-Ph	24.7
1-Ph	0.537

It is at once clear that the transition state reflects the importance of the C-C scission over the C-H formation. Therefore, C-O π bond develops subsequent to the 2-3 π system. Thus the 4 substitution favourably influences the reaction. The profound effect of 2-phenyl may be related to the stabilization of the developing 2-3 π at the transition state. The severe retardation in the case of 1-Ph is general for reactions proceeding *via* a cyclic transition state. In the ene reaction the transition state reflects the C-C bond formation over the O-H.[6]

Interestingly, for the related fragmentation,

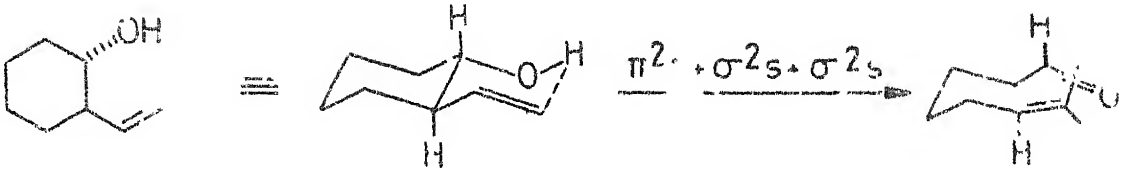


the rate is enhanced five-fold[5], thus enabling a comparison of β,γ -unsaturated acid fragmentation with γ,δ -unsaturated alcohol rupture.

An ingenious set of experiments[7] has helped in the visualization of the transition state in these fragmentations. trans-2-Vinyl cyclohexanol on thermolysis gives exclusively the E olefin. In sharp contrast cis-2-vinyl alcohol gives an almost equal mixture of E and Z olefins. This observation can be beautifully explained in terms of a chair-like transition state for the fragmentation (CHART II.B.2).

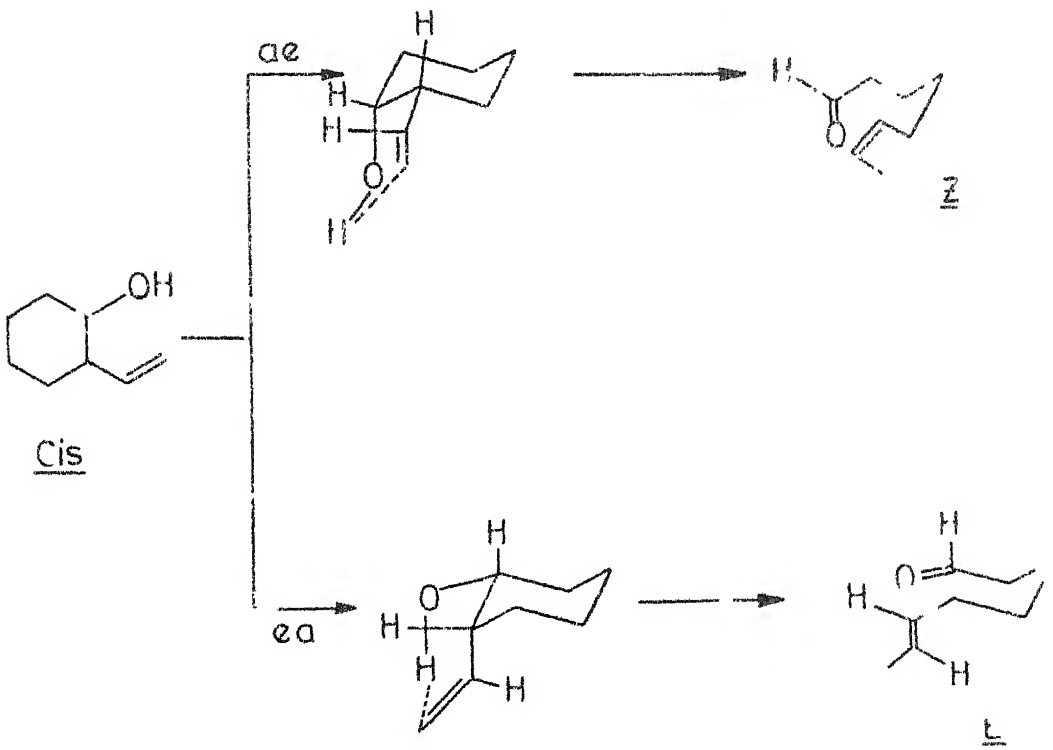
Experiments permitting a competition of the retro-ene reaction ($\pi^2s + \sigma^2s + \sigma^2s$) with the more popular Cope reaction ($\pi^2s + \pi^2s + \sigma^2s$) have further sharpened the understanding of the γ,δ -unsaturated alcohol fragmentation, particularly with respect to the influence of substituents.[8] Whereas, in the parent system, hexa 1,5-diene 3-ol, the Cope is favoured over retro-ene (60:40), a single methyl substitution at the 1-position

CHART II B 2



trans

E-only



Cis

Z

E

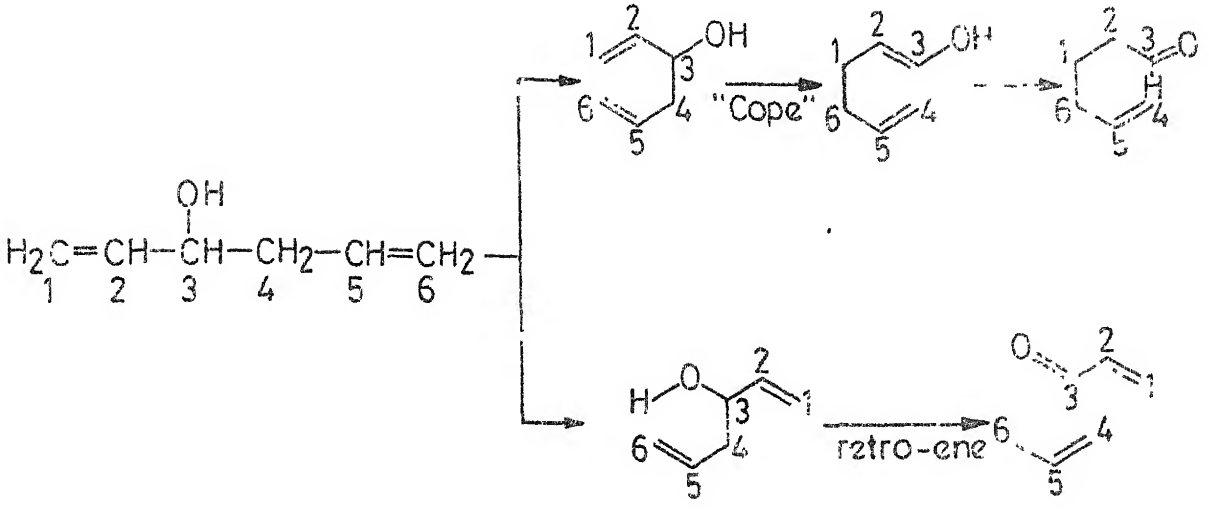
(a Cope terminus), dramatically changes the ratio to 29:70, and a bis substitution to practically retro-ene (4:96) (CHART II.B.3)!

The spatial constraints related to the retro-ene are perhaps less restrictive compared to the Cope rearrangement. This inference can be drawn from the fact that the acetylenic analog of retro-ene is distinctly favoured over the corresponding Cope as illustrated with the thermal fragmentation of 3-methyl 3-hydroxy hex 1-ene 5-yne[9] (CHART II.B.4).

Amongst natural products, castor oil by no means is the only case where the retro-ene was noted. Indeed, there are delightful transformations recorded in the terpene area. As early as 1927, Triebs and Schmidt[10] observed that the abundantly available citronellal undergoes cyclization to pulegol at 350°C. Three years later, Grignard and Doeuvre[11] discovered that pulegol can be thermally transformed at 500° to citronellal! The forward process is an ene reaction and the reverse the retro-ene, characteristic of γ,δ-unsaturated alcohols. As a rule, higher temperatures favour the retro-ene process. Whilst currently the citronellal ⟶ pulegol change is brought about preferentially using a variety of catalysts under mild conditions,[12] the pulegol ⟶ citronellal transformation is best done by a thermal retro-ene fragmentation[13] (CHART II.B.5.a).

Hydroxymethyl Δ^4 carene incorporates facets that permit two types of $\pi^2s + \sigma^2s + \sigma^2s$ changes, one of which is the

CHART II B 3



Methyl position	Cope (%)	retro-ene (%)
0	60	40
1	29	70
2	64	36
3	65	35
4	66	33
5	33	67
4,6	55	45
1,5	12	88
2,5	25	75
3,5	42	58
1,1,3	4	96

CHART II B 4

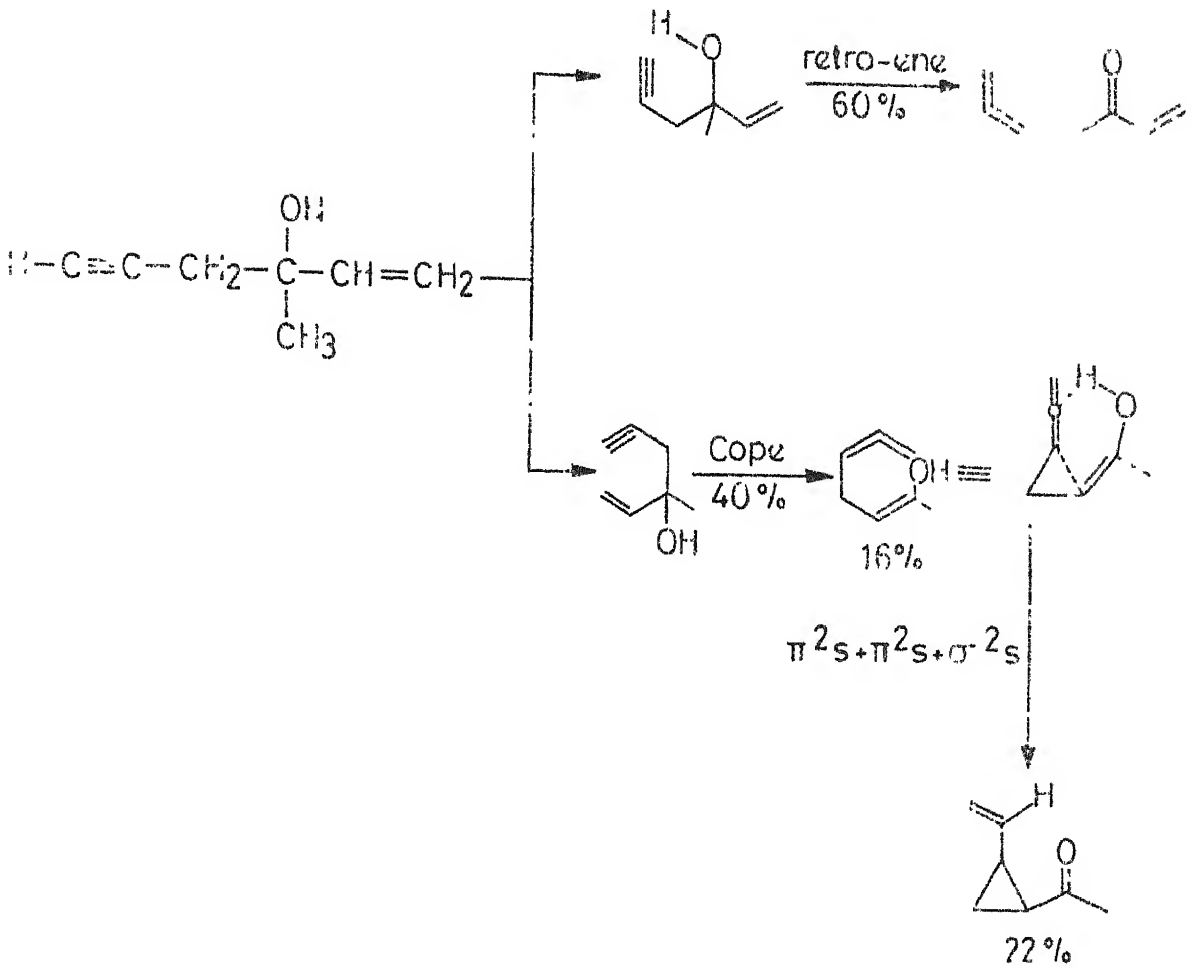
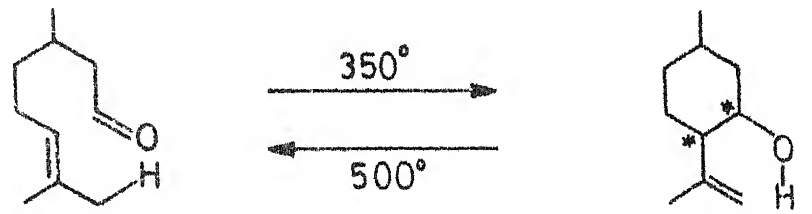


CHART II.B 5

γ,δ-unsaturated alcohol fragmentation in monoterpenes

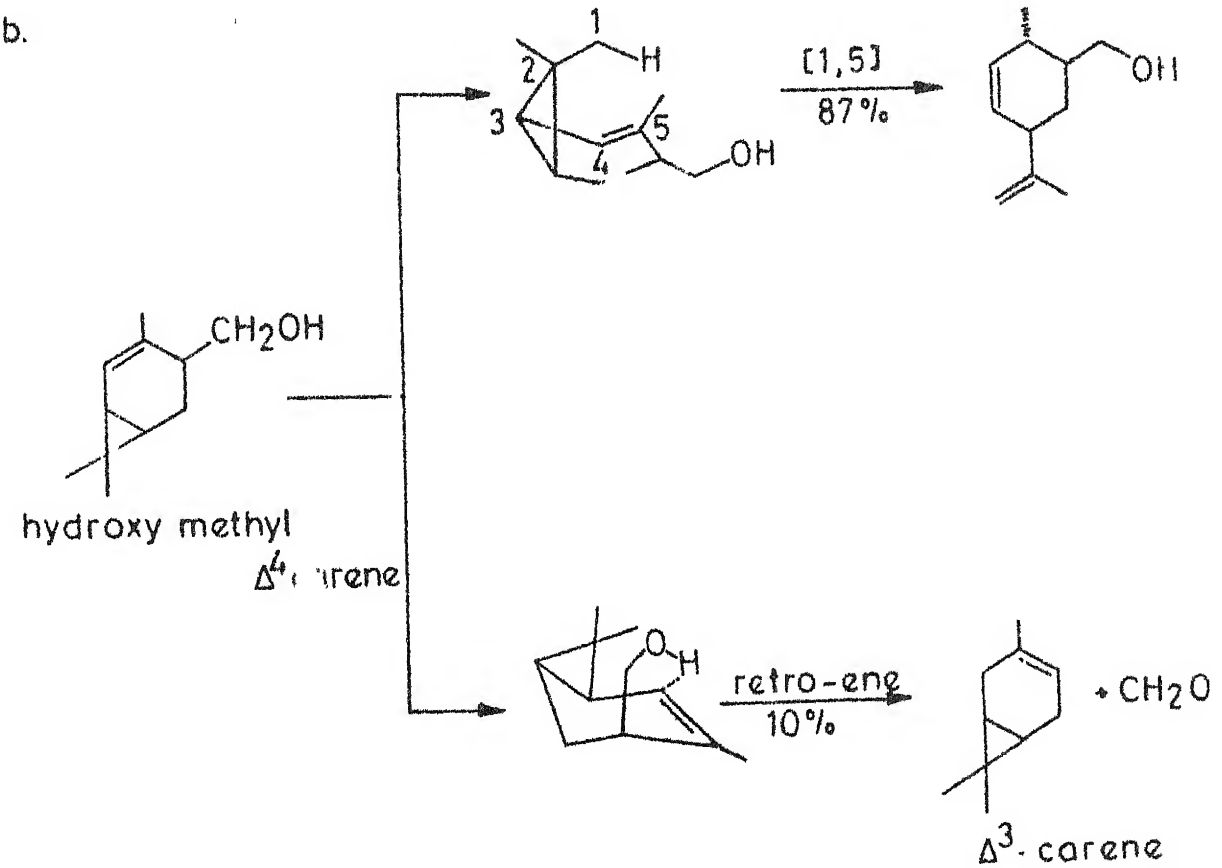
a



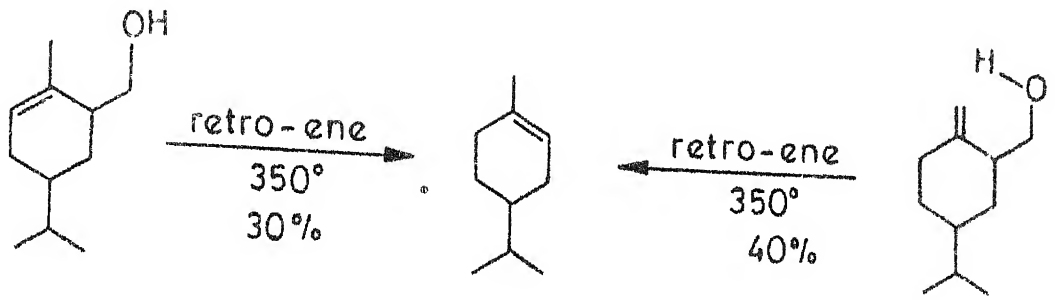
* mixtures

Citronellal — Pulegol

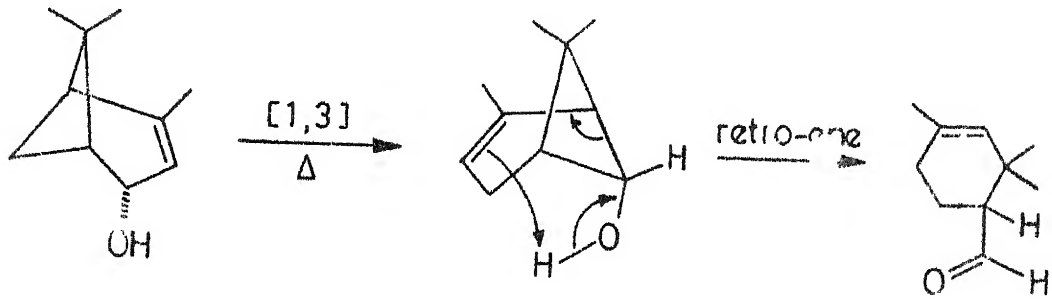
b.



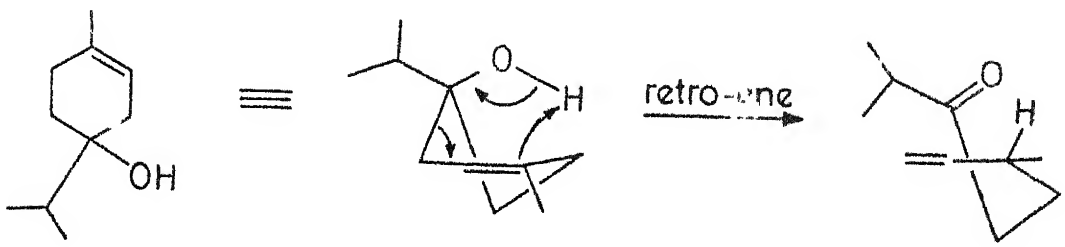
Δ3-carene



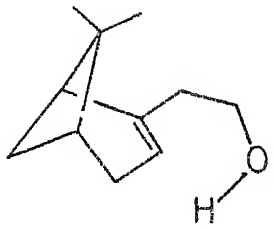
c.



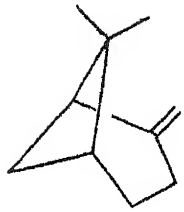
trans-verbenol



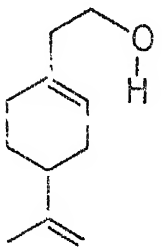
d.



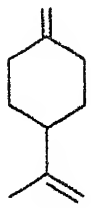
retro-ene →



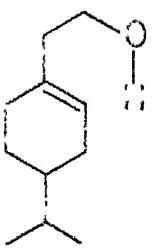
+ CH_2O



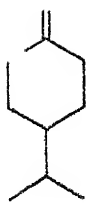
retro-ene
88 %



+ CH_2O



retro-ene →



+ CH_2O

(1,5) sigmatropic shift and the other a retro-ene reaction. In the event, thermolysis gives rise to products arising from both the processes in the ratio, (1,5): retro-ene::87:10.[14] The retro-ene reaction gives rise to Δ^3 carene (CHART II.B.5.b). trans Verbenol is thermally transformed to the product arising from sequential (1,3) shift and retro-ene reaction[15,16] (CHART II.B.5.c). Nopol, an industrial product from β -pinene and formaldehyde undergoes the retro-ene reaction on boiling. This observation has been taken advantage of, for novel routes to menthene and menthadiene[17] (CHART II.B.5.d).

One of the goals relating to our own study of thermolysis of the γ ,δ -unsaturated alcohol system (SECTION II.C) is to develop this reaction as a tool in synthesis. Few reports thus far available demonstrate the practical potential of this fragmentation. The first application of γ ,δ -unsaturated alcohol fragmentation is related to the transformation of cyclic olefins to open chain aldehydes.[18] The required homoallyl alcohol is generated via sequence, epoxide formation, acetylide opening and hydrogenation. Pyrolysis of the resulting compounds gave ring fragmentation products by retro-ene process (CHART II.B.6). The method suffers from factors such as poor yields in the acetylide opening stage and the presumable lack of control in the π bond formation. The process deserves re-examination with synthetic tools and improved analytical

CHART II B 6

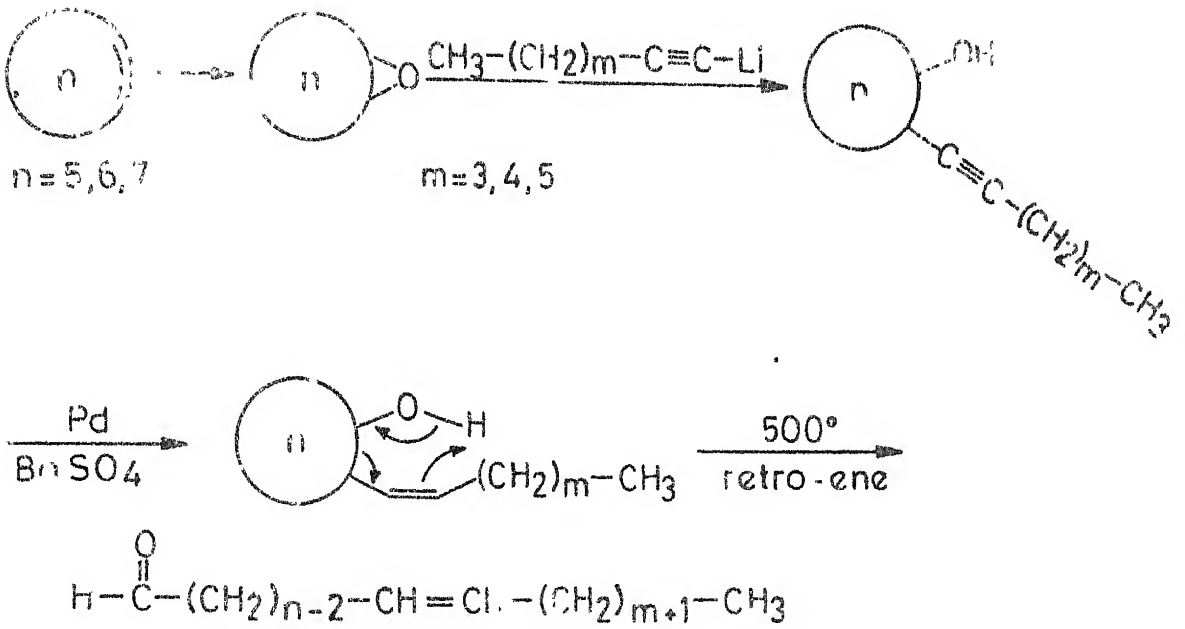
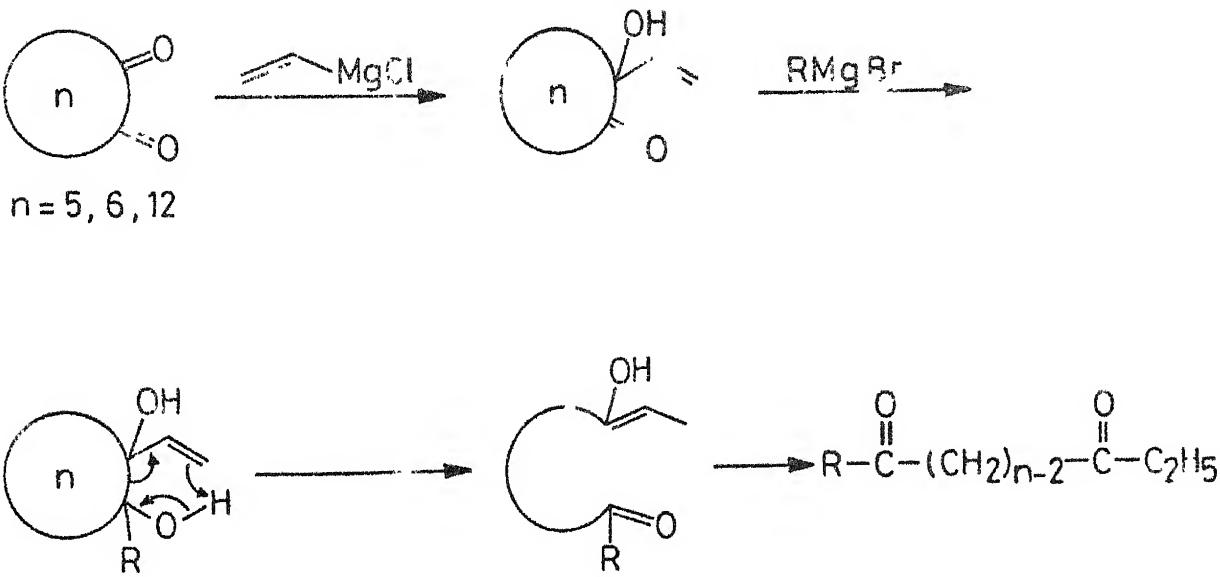


CHART II B.7.



techniques currently available. Attempts to demonstrate the retro-yne process of γ,δ-unsaturated alcohol, with the acetylide opened product, failed. In the present work we have been able to demonstrate the retro-yne process leading to allene formation (SECTION II.C). A related fragmentation that proceeds well, is the transformation of cyclic 1,2-diketones to open diones. The requisite γ,δ-unsaturated alcohol is generated by selective addition of vinyl Grignard followed by either reduction or alkyl Grignard addition to the remaining carbonyl group [19] (CHART II.B.7). The retro-ene reaction has been elegantly used in the removal of the D-ring acetyl group in steroids [19] (CHART II.B.8).

The attachment of a 6 carbon unit having a functional aldehyde end has been accomplished by this fragmentation. Thus the chlorine equivalent of cyclohexanone aldol-available from cyclohexanone and HCl - leads to the γ,δ-unsaturated alcohol system <u>via</u> HCl elimination and either reduction or Grignard addition. The resulting compounds undergo smooth retro-ene on thermolysis[20] (CHART II.B.9).

CHART II.B 8.

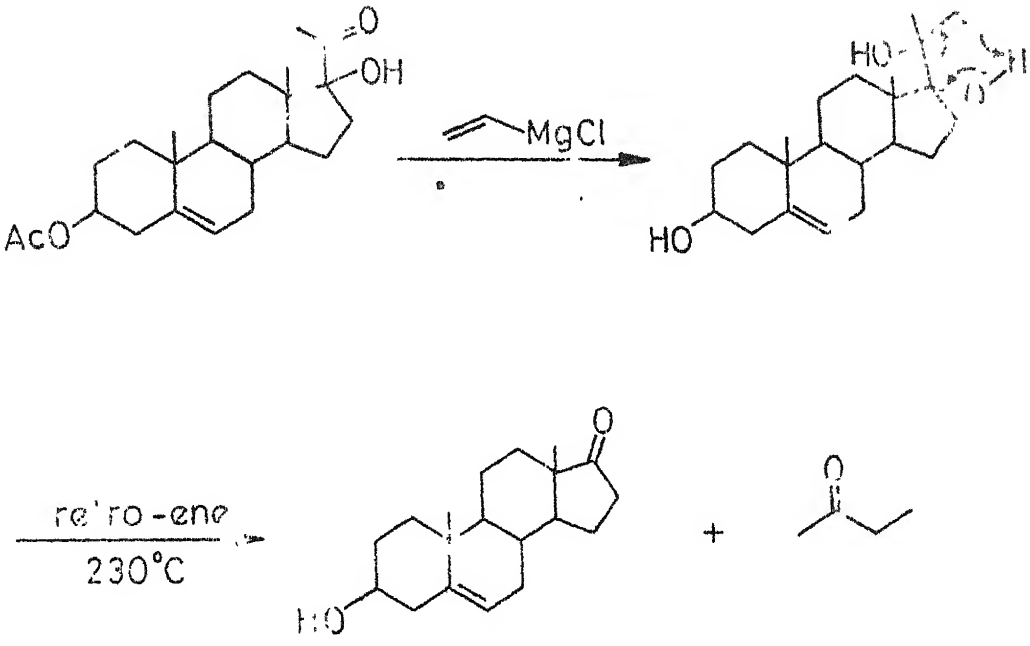
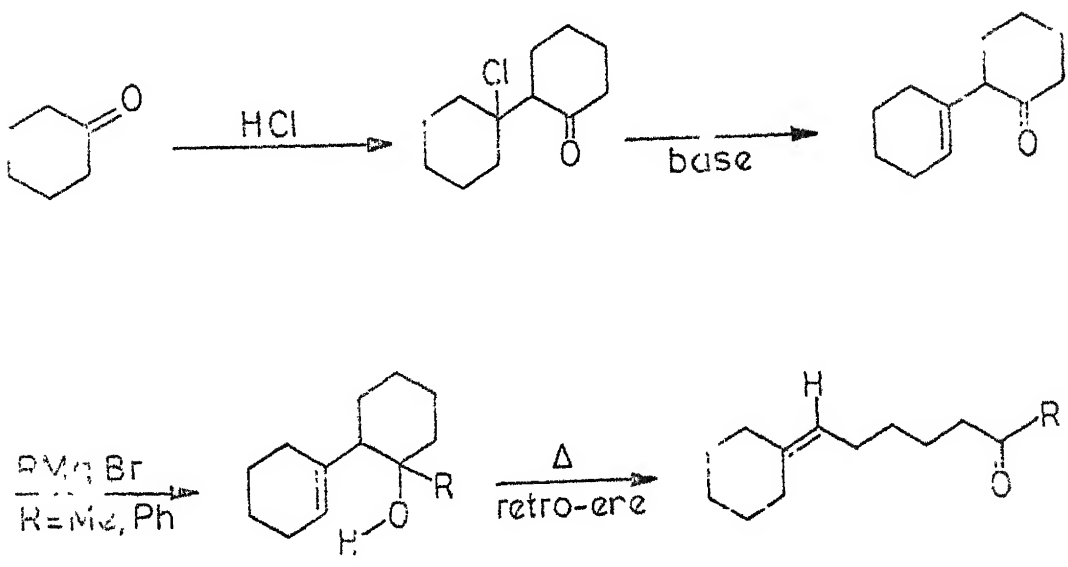


CHART II B.9



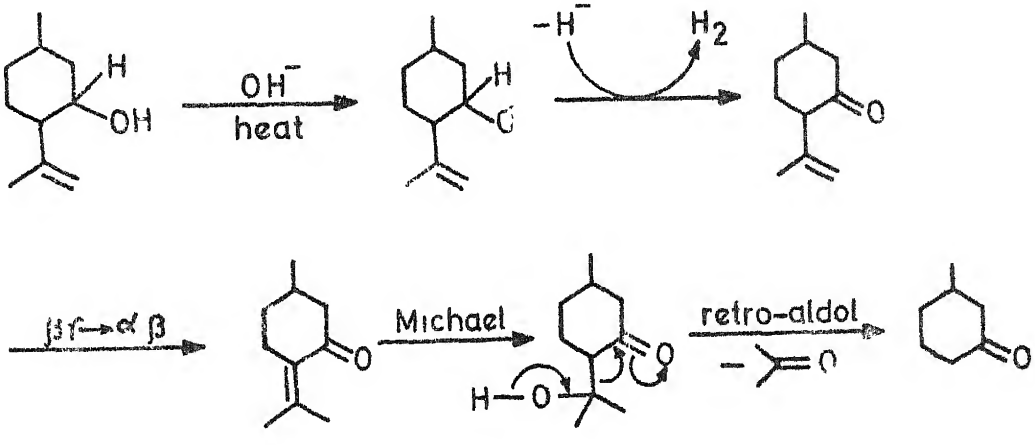
Thermolysis of homoallylic alcohols under "basic" conditions

Practically all the knowledge relating to the alkaline thermolysis of the γ ,δ -unsaturated unit comes from studies on castor oil. These will be presented in the course of discussion of the present work on this subject (SECTION II.C). The reaction is immensely complicated and the nature of products is very much related to diverse factors, such as "alkalinity" of the medium, temperature and the nature of additives. In the case of ricinoleic acid, the reactions of the γ , δ -unsaturated alcohol unit become superposed by incursion of Varentrap reaction that leads to degradation from the carboxyl end ! Indeed, there appears only one example wherein the γ , δ -unsaturated alcohol unit is not encumbered by ligands that would further complicate the reaction. This report is in the form of an obscure communication and deserves closer scrutiny. Under alkaline conditions iso-pulegol is transformed to 3-methyl cyclohexanol.[21] This profound change can be rationalized *via* sequence, the oxidation of the secondary hydroxyl to ketone by hydride loss, the transformation of the resulting β , γ -unsaturated ketone to α , β . Michael addition of elements of hydroxide, the retro reaction of the resulting aldol leading to 3-methyl cyclohexanone and the reduction of the latter to the product, 3-methyl cyclohexanol ! The reduction takes place by operation of redox system having the starting alcohol as the partner (CHART II.B.10).

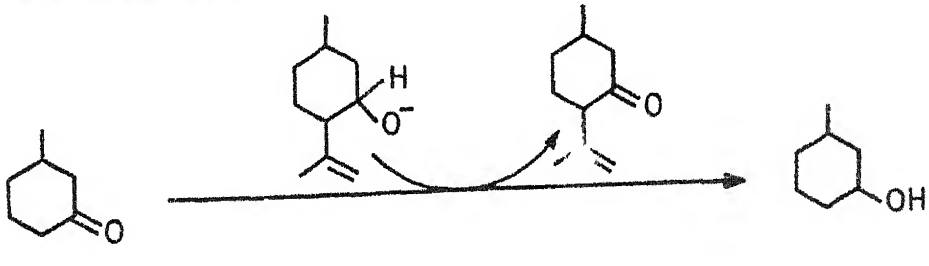
CHART II.B.10

The transformation of iso-pulegol to 3-methyl cyclohexanol with alkali

Primary process



Redox system

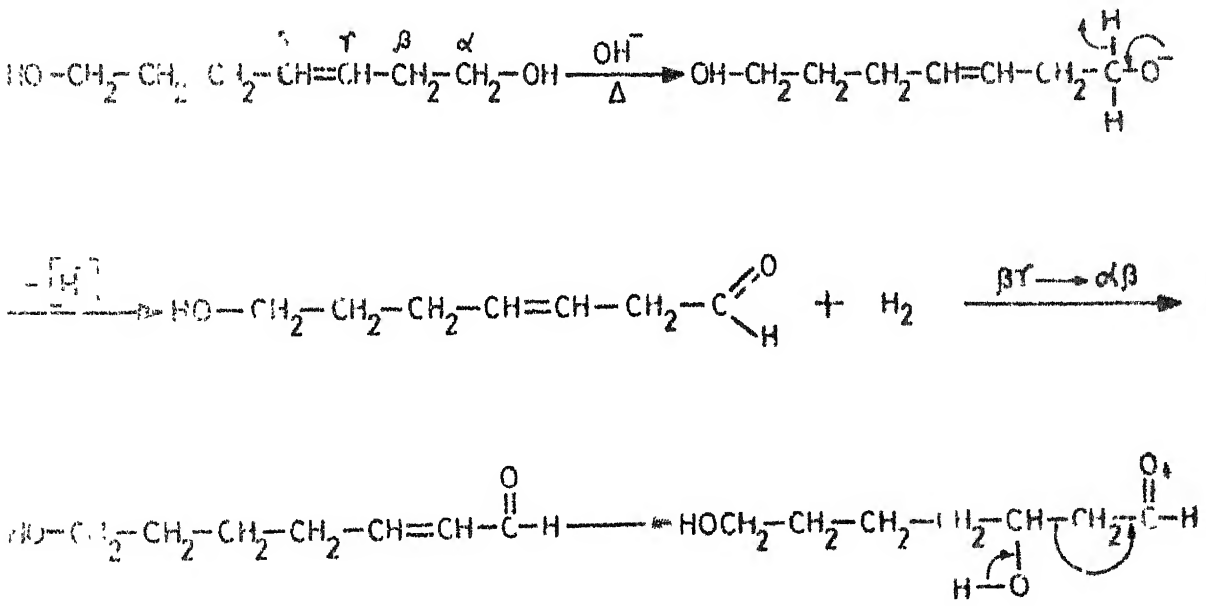


The thermolytic cleavage of pent 3-ene 1,7-diol, possessing a γ, δ-unsaturated alcohol unit, under alkaline conditions to glutaric acid and acetic acid[22] has facets common to the castor oil cleavage under similar conditions. However, since coupled redox processes are not present the substrates are oxidized with release of hydrogen (CHART II.B.11). Generally, high temperatures favour uncoupled oxidation of the aldehyde moiety whereas, at lower temperatures it forms part of a redox system coupled with alcoholic substrates present in the medium.

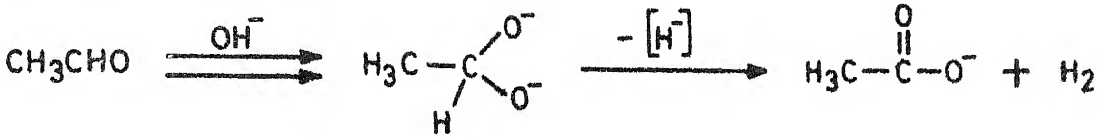
The primary reaction that sets in motion a variety of further changes is the alcohol $\longrightarrow$ carbonyl group transformation. In the case of γ, δ-unsaturated alcohols the resulting β, γ-ketones will rapidly be changed to the α, β-unsaturated ketones. In the case of allylic alcohols - β, γ-unsaturated alcohols - the hydride release would directly lead to the α, β-unsaturated ketones. Consequently, allyl alcohols could also be anticipated to give products similar to homoallyl alcohols on heating with alkali. This is the case. A very early fascinating example is the transformation of geraniol to 6-hydroxy 2-methyl 2-heptene.[23] This unusual transformation can be rationalized by pathways similar to that envisaged for the iso-pulegol $\longrightarrow$ 3-methyl cyclohexanol change (CHART II.B.12).

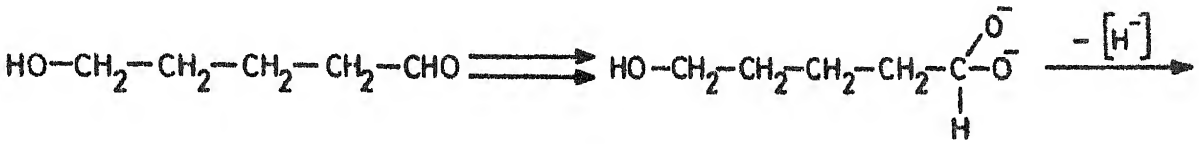
CHART II.B.11

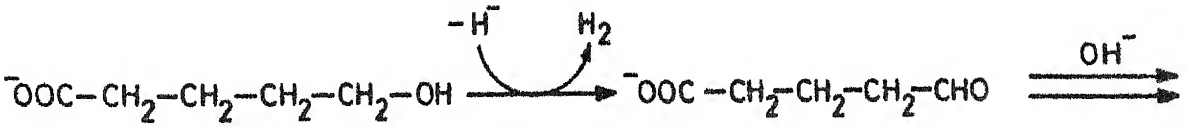
Primary process

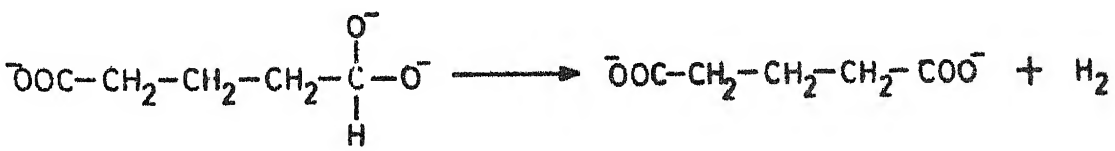


Uncoupled oxidation









Overall reaction

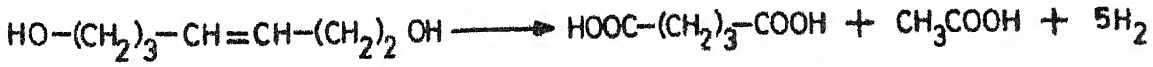
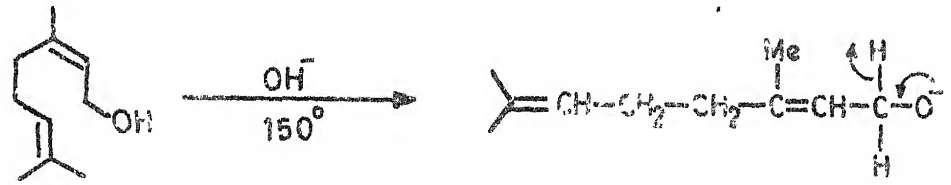
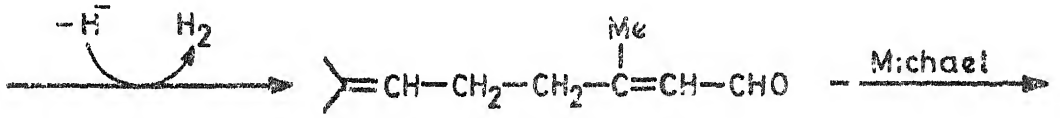


CHART II.B.12

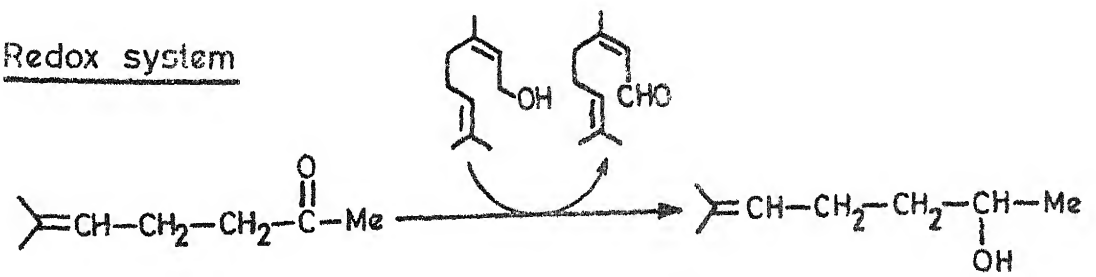
Primary process



geraniol



Redox system

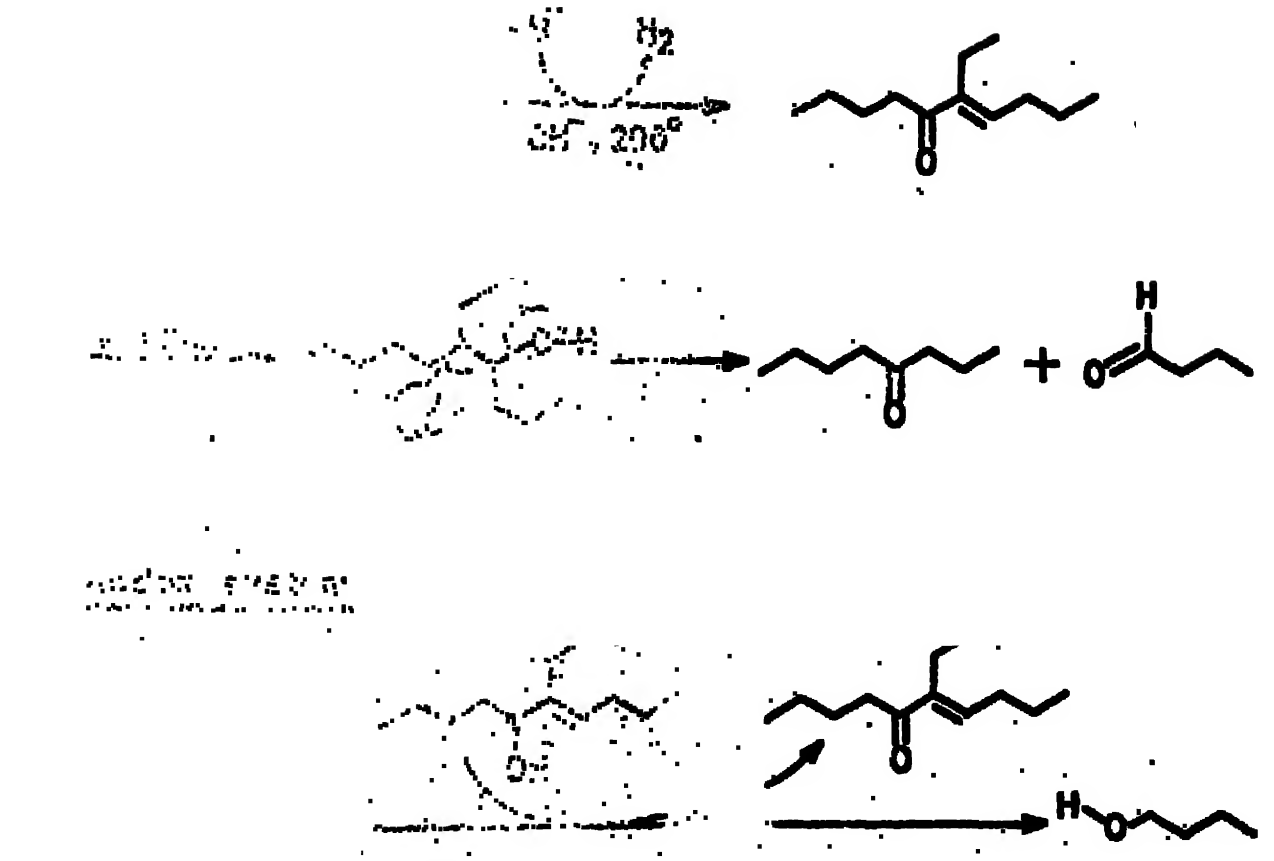


The alkali mediated cleavage of allyl alcohol models.[24]

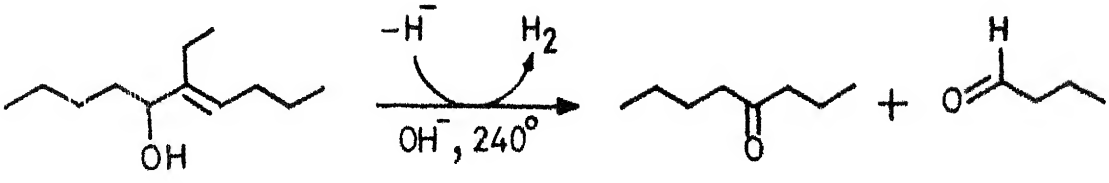
A particularly noteworthy illustration is the alkaline fragmentation of 6-hydroxy 5-ethyl dec 4-ene. At 200°C the reaction leads to 4-octanone and n-butanol, presenting a nearly perfectly coupled redox system (CHART II.B.13.a). In sharp contrast, at 240°C, uncoupled oxidation takes place giving rise to 4-octanol, butyric acid and hydrogen (CHART II.B.13.b). Precisely similar events take place at 240°C in the case of 3-hydroxy oct 2-ene leading to 2-hexanol, acetic acid and hydrogen[24] (CHART II.B.13.c).

The potential of the γ,δ -unsaturated alcohol unit in synthetic strategy largely remains untapped. The available information has been presented in this section in an integrated manner that would make the utility of this system hopefully more apparent.

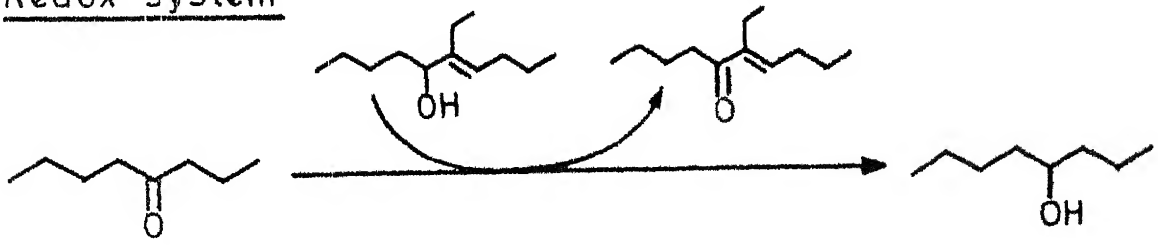
CHART II.B.13



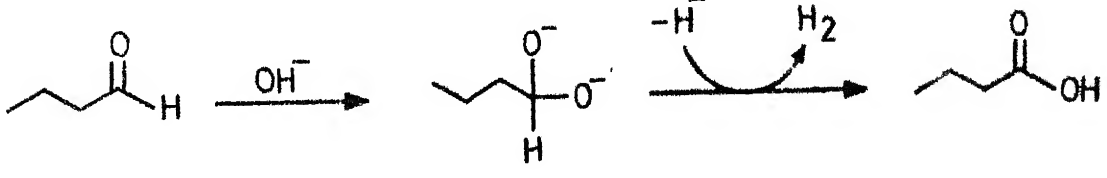
b. Primary process



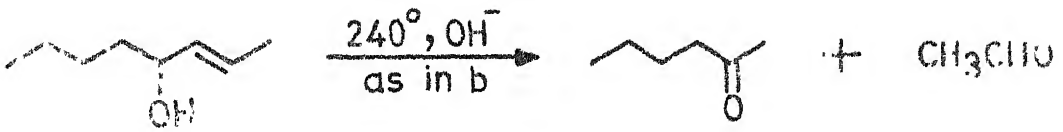
Redox system



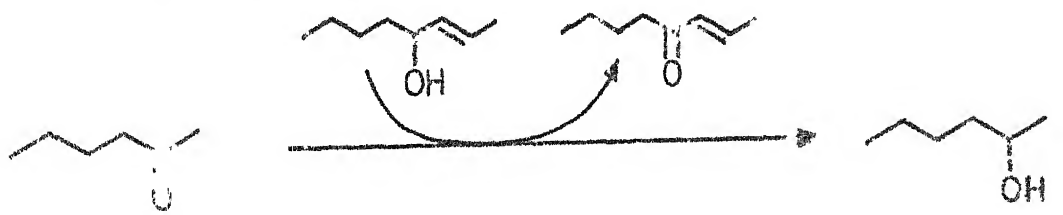
Uncoupled oxidation



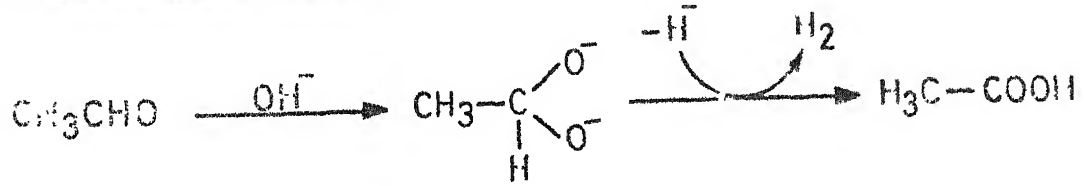
imary process



Redox system



Uncatalyzed oxidation



II.C. PRESENT WORK

The rupture of the C-18 backbone of castor oil, thermally, under neutral conditions to C-11 + C-7, on the one hand, and with alkali to C-10 + C-8 on the other, is of significance, since, almost all of the very many synthons that owe their genesis to this unusual, yet abundant, natural product, and which have found applications in the diverse facets relating to the use of carbon constellations in the current state of social development, arise from this fragmentation. Inspite of their obvious importance, these scission pathways have not been examined in the light of recent advances relating to the understanding of bond-forming and bond-breaking interactions with carbon substrates. The present work was undertaken with such an objective. Information thus far available has been augmented with that from the present study and this has enabled the development of an integrated picture, which from mechanistic as well as practical viewpoints should be useful.

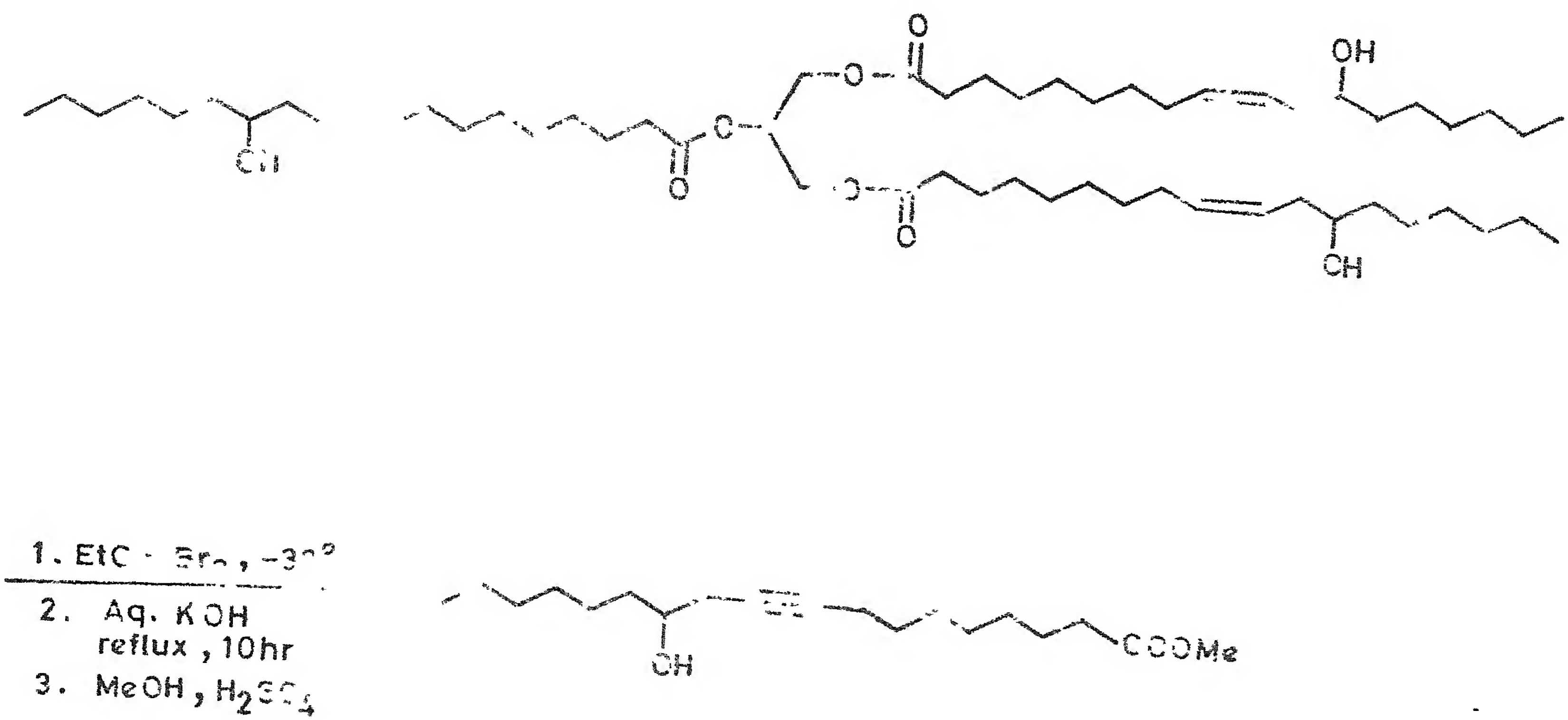
The thermal C-18 ⟶ C-11 + C-7 fragmentation of castor oil

Castor oil is thermally transformed to heptaldehyde and undecenoic acid. The related scission of methyl ricinoleate is

more practical and a reliable recipe for this is already presented in I.E.

This fragmentation was first discovered in 1827 and Barbot[1] with commendable intuition proposed in 1935 that it proceeds by a six membered transition state, much as we understand to-day, as a result of studies on model systems (SECTION II.B). With the advent of Woodward - Hoffmann rules, the reaction can be understood as a $\pi^2s + \sigma^2s + \sigma^2s$ process, which is popularly known as the retro-ene reaction. However, studies directed at the establishment of the retro-ene pathway in the ricinoleic acid system itself have not been made thus far. The thermal fragmentation of methyl 12-hydroxy 9-undecynoate (3) was therefore examined. The "retro-ene" pathway would give rise to the novel allenic ester 4. On the other hand, fragmentation by non-concerted modes would give mixtures, largely comprising of acetylenic products. An additional attractive feature is that, thus far a $\pi^2s + \sigma^2s + \sigma^2s$ pathway has not been experimentally demonstrated for γ, δ-unsaturated acetylenic alcohols. The acetylenic acid 2 was directly prepared from castor oil, by a modified procedure,[25] *via* sequence, low temperature bromine addition and elimination with potassium hydroxide in an overall yield of 85%. The acid was transformed to the methyl ester 3 in 95% yields with MeOH + H_2SO_4 (CHART II.C.1).

SCHEME 1



2: mp 47°; ir: ν_{max}(neat)(cm^{-1}): 3468 (hydroxyl), 1710(acid).

3: bp 130-135°/0.05 torr; ir: ν_{max}(neat)(cm^{-1}) 3420 (hydroxyl),1740(ester).

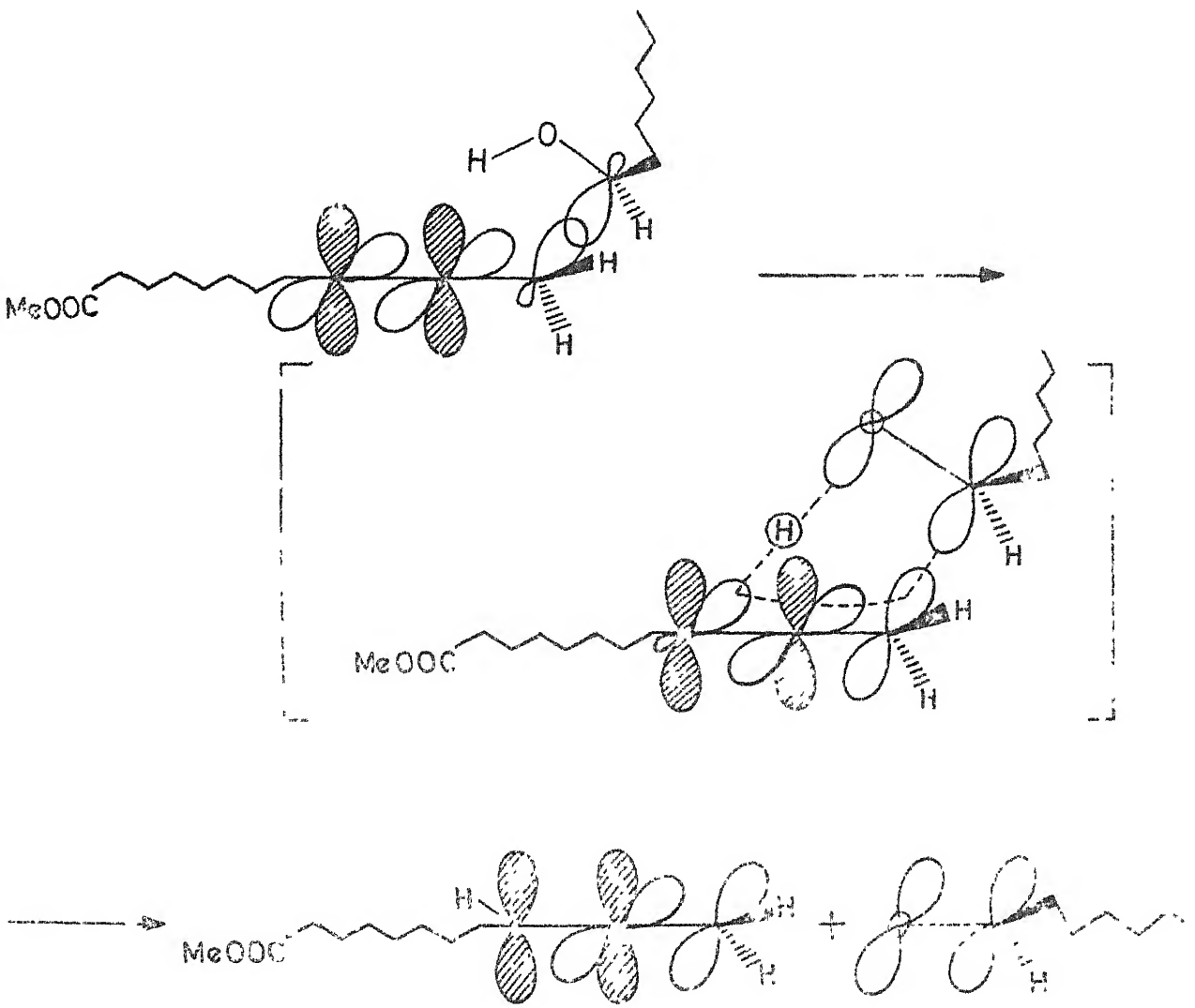
The methyl ester 3, on thermolysis underwent, surprisingly smooth fragmentation leading to the allenic ester 4 in 71% yields. The transformation was clean and no acetylenic products could be detected. A comparison of the $\pi^2s + \sigma^2s + \sigma^2s$ processes involving the olefinic system, methyl ricinoleate, and the acetylenic compound, methyl 12-hydroxy 9-undecynoate clearly show that the latter is a better substrate for the scission. This may be due to the operation of a relaxed transition state for the retro-ene reaction in the case of γ,δ-acetylenic alcohols (CHART II.C.2) or may as well be because of diminished tendency for elimination, which is the major competing pathway in the castor oil pyrolysis (vide infra).

4: bp 75-78°/0.07 torr

ir : ν_{max}(neat)(cm^{-1}): 1950 (allene), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 2.15 m, (4H, $-C\underline{H}_2COOCH_3$, $=CH-C\underline{H}_2-$), 3.5 (s, 3H, $-COOC\underline{H}_3$), 4.45 (qq,2H, $C\underline{H}_2=C=C-$), 4.9 (m, 1H, $CH_2=C=C\underline{H}-CH_2$).

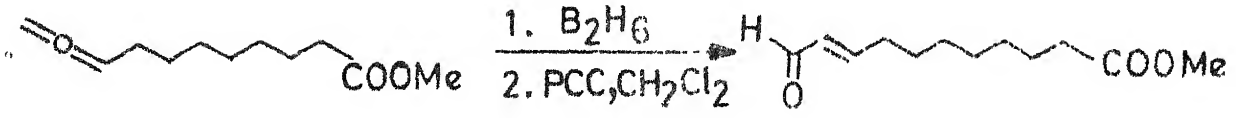
CHART II.C.2



The usefulness of 4 as a readily available synthon is yet to be explored. That this could be considerable has been demonstrated by its transformation to methyl 11-oxo (E) 9-undecenoate (5) by hydroboration-oxidation (CHART II.C.3). Compound 5 is a precursor for insect sex pheromones (SECTION I.C) and prostaglandin homologs.[26] Further, the 3 $\longrightarrow$ 4 change has opened up a novel route for the transformation of terminal acetylenes to higher allenes via 2-hydroxy ethylation with ethylene oxide followed by thermolysis of the resulting γ, δ-unsaturated acetylenic alcohols.

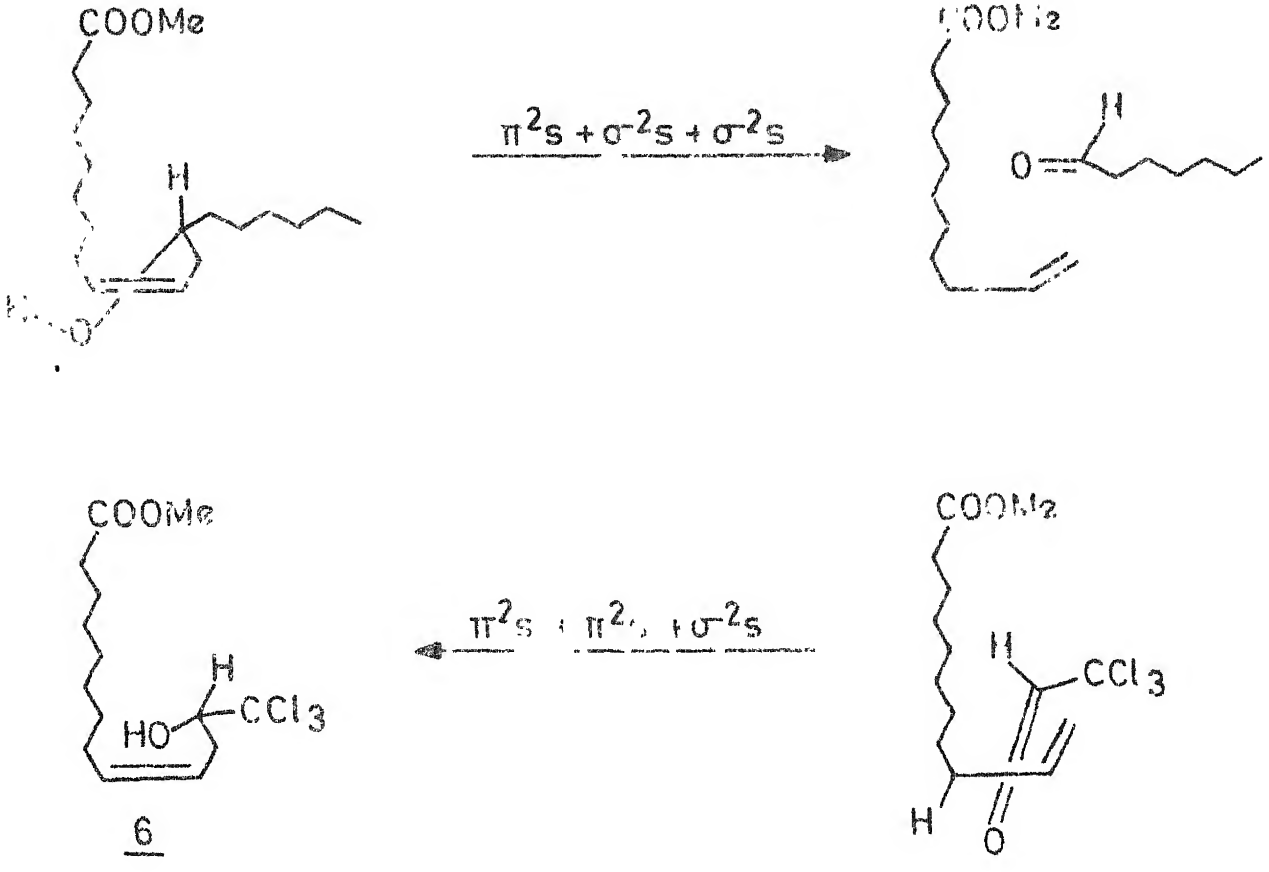
The favoured direction of the ene $\rightleftharpoons$ retro-ene system should, in principle, be a function of the nature of the participant(s) and the reaction conditions. Whilst the ene reaction underscores the importance of the C-C bond formation to the transition state, the retro-ene highlights the C-C rupture ! Thus, electrophilic π systems and lower temperatures promote the ene process, on the other hand, electron donating substituents and higher temperatures favour the retro-ene. Therefore it should be possible to bring about a unit replacement via sequence, retro-ene ($\pi^2s + \sigma^2s + \sigma^2s$), ene ($\pi^2s + \pi^2s + \sigma^2s$). For example, this strategy would enable the replacement of the C_{12}-C_{18} moiety of castor oil with another unit. Thus, methyl 12-hydroxy 12-hexyl 9-dodecenoate (methyl ricinoleate, 1) should lead to methyl 12-hydroxy 12-trichloromethyl 9-dodecenoate by

CHART II.C.3



4 5

CHART II.C.4



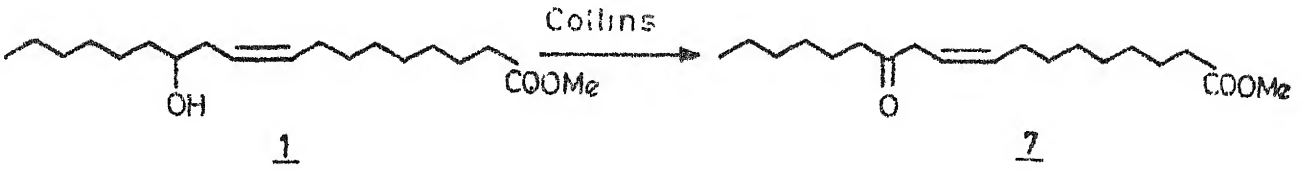
6

retro-ene followed by ene reaction involving the resulting methyl 10-undecenoate with chloral (CHART II.C.4). It has been reported recently[27] that 1-hexene and 1-octene, having features similar to methyl 10-undecenoate, undergo ene reaction with chloral giving rise to adducts, possessing a terminal hydroxy-trichloromethyl grouping and which can be readily transformed to a variety of synthons.

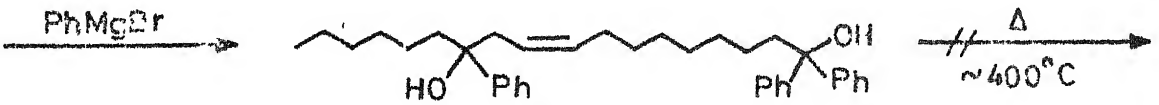
In the event, the reaction of methyl 10-undecenoate with chloral (CHART II.C.4) was found to be complex and a careful analysis indicated no chloral incorporation. Extensive de-esterification was observed.

The 10-undecenoic acid $\longrightarrow$ 9-decenoic acid change by Barbier Wieland degradation is a key step in the synthesis of prostaglandins and insect sex pheromones (SECTION I.C). It was felt that 1,1-diphenyl undeca 1,10-diene (9), a precursor to 9-decenoic acid could arise directly from the retro-ene fragmentation of diol 8, which, in turn, could be readily prepared from methyl ricinoleate (1) (CHART II.C.5). It was anticipated that the $\pi^2s + \sigma^2s + \sigma^2s$ process of the γ,δ-unsaturated alcohol unit in 8 would be more facile because of enhanced tendency for the key C-C rupture. In the event, however, thermolysis of 8 led to total dehydration leading to the novel 1,1,12-triphenyl 1,9,11-octadecatriene (10).

CHART II.C.5



1 7



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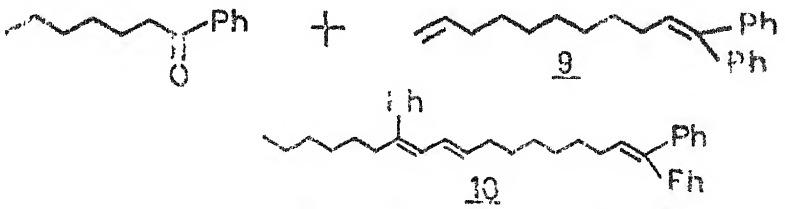
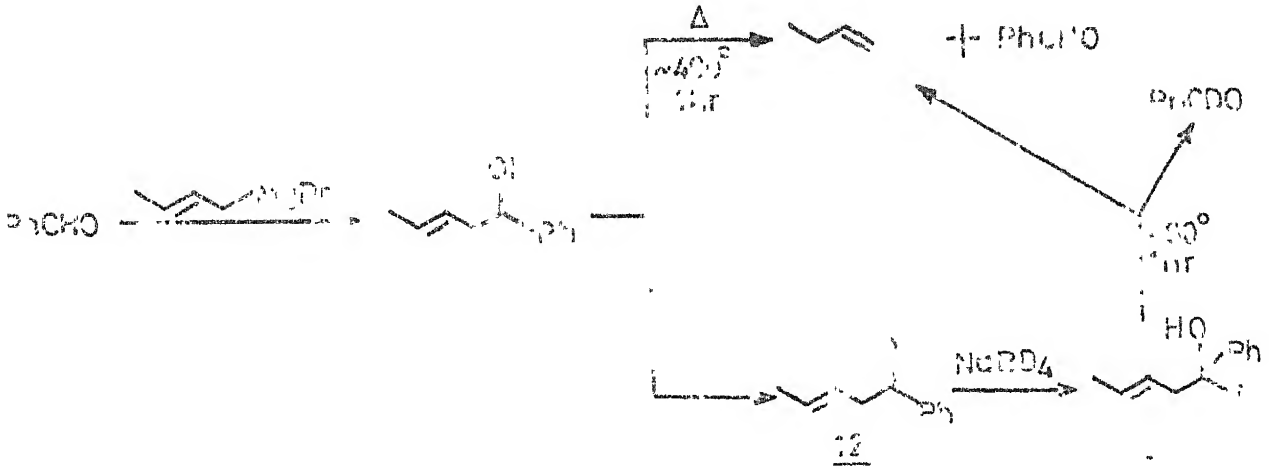


9 10

CHART II.C.6



12

ir : ν_{max}(neat)(cm^{-1}): 1650, 970 (double bond), 1600 (phenyl).

Additional facets of the γ,δ -unsaturated alcohol fragmentation were examined with a view to, not only supplement the existing knowledge in the area (SECTION II.B), but also to enable the generalisation of the castor oil cleavage from the point of efficiency and the formation of novel fragmentation products.

The $\pi^2s + \sigma^2s + \sigma^2s$ fragmentation of γ ,δ -unsaturated alcohols have been taken advantage of to develop a novel and simple procedure for the R-C(=O)-H ⟶ R-C(=O)-D transformation. Thus, the Ph-C(=O)-H ⟶ Ph-C(=O)-D change has been accomplished, in good yields, via sequence, crotyl Grignard addition, PCC oxidation, $NaBD_4$ reduction and thermolysis (CHART II.C.6).

Whilst it is accepted that the "retro-ene" fragmentation of γ ,δ -unsaturated alcohols should be assisted by α-substituents that would promote the α - β C-C scission, the nature of the polarization of this bond, if any, has not been experimentally demonstrated. Therefore the $\pi^2s + \sigma^2s + \sigma^2s$ fragmentation of γ ,δ -unsaturated alcohols that carry an α -aryl substituent was studied under identical conditions and the ease of scission assessed in terms of isolated yields of the aromatic aldehydes.

The results are presented in CHART II.C.7. The dramatic increase in the yield of scissionproducts in the case of the α-toluyl substituent is a clear indication that the anticipated $C_{\beta} \overleftarrow{-} C_{\alpha}$ polarization is real. The diminished tendency for fragmentation exhibited by the α-p-nitrophenyl substituent is also in accord with this conclusion. Therefore substitution of the α position of γ, δ-unsaturated alcohols with efficient electron releasing substituents would enable the retro-ene fragmentation under comparitively mild conditions, thereby increasing the yield of products. Such substitution can be easily brought about, as described in the present work, by PCC oxidation followed by Grignard addition.

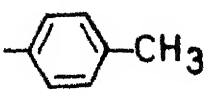
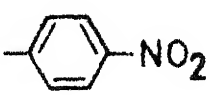
Thermolysis of castor oil under "basic conditions"

Although the cleavage of castor oil on thermolysis under alkaline conditions to sebacic acid and octanol is known since 1851, the multifacetted aspects of this delightful and fascinating transformation have not been captured in a single mural. Such a picture has emerged in the present work, which illustrates, inter alia, hydride transfer, π-migration, Michael addition, Meerwein-Ponndorf-Verley-Oppenauer redox systems, Cannizzaro reaction and uncoupled substrate oxidations.

The first comprehensive scrutiny of the alkaline scission of castor oil was reported by Hargreaves and Owen[24] in 1947.

CHART II.C.7

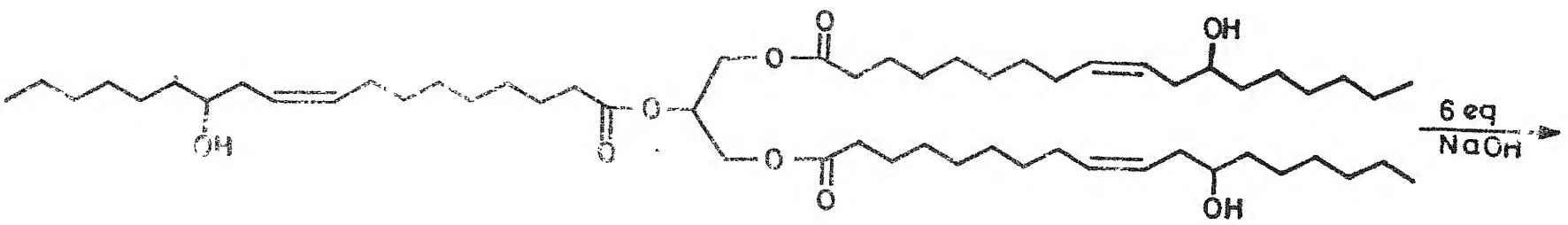
Thermolysis of γ,δ-unsaturated alcohols at 400°C for 1hr

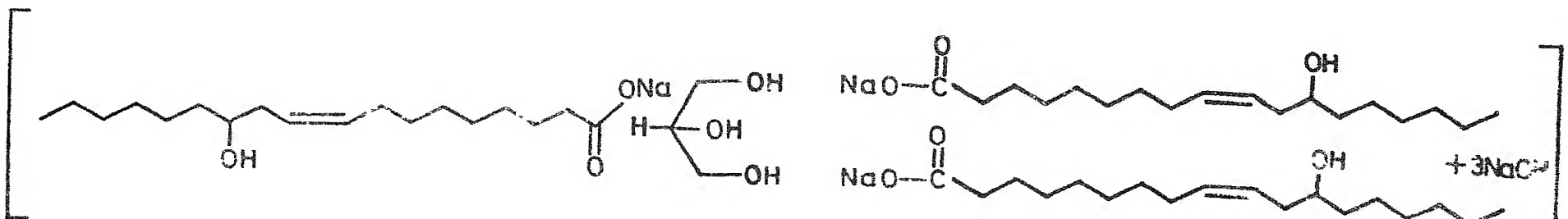
No.	R	R'	Isolated yield (%)*
14	H	Ph	39
15	H		71
16	H		18**
17	Me	Ph	57

* Yield, not taking into account recovered starting material, based on semicarbazones.

** Yield of crystalline aldehyde

CHART II.C.8





castor soap 18

In the course of this analysis, several significant observations were made. The course of the cleavage could be controlled as a function of the temperature at which the reaction is carried out. Thus, in 60% NaOH ricinoleic acid was transformed at 180° to 10-hydroxy decanoic acid (19) + 2-octanone (21) and under the same conditions, at 240°, to 1,10 decanedioic acid (sebacic acid, 20) and 2-octanol (22). Additionally, when the 19 + 21 mixture was heated to 240°, it was transformed to 20 + 22 (CHART II.C.9). Practically no hydrogen evolution was observed at 180°. However, this became significant at 240°. Thus the 19 ⟶ 20 change is shown to be associated with an uncoupled oxidation step. Hargreaves and Owen incorrectly surmised that the first step was an γ,δ-unsaturated alcohol ⟶ α,β-unsaturated alcohol. The allyl alcohol thus formed was envisaged to undergo oxidation *via* loss of elements of hydride. The resulting α,β-unsaturated ketone would, *via* Michael addition followed by retro-aldol cleavage, give 2-octanone (21) and 10-oxo decanoic acid. An extensive examination of the reactions that take place at high temperatures in strong alkali relating to a variety of substrates related to fatty acids, by Weedon and co-workers[28] has shown that unactivated secondary hydroxyl functions are oxidised to ketones under conditions of the castor oil cleavage. Consequently, the primary, rather implausible, homoallyl alcohol ⟶ allyl alcohol change, envisaged earlier, is not needed. On the contrary, the β,γ-ketone arising from the primary step of

CHART II.C.9

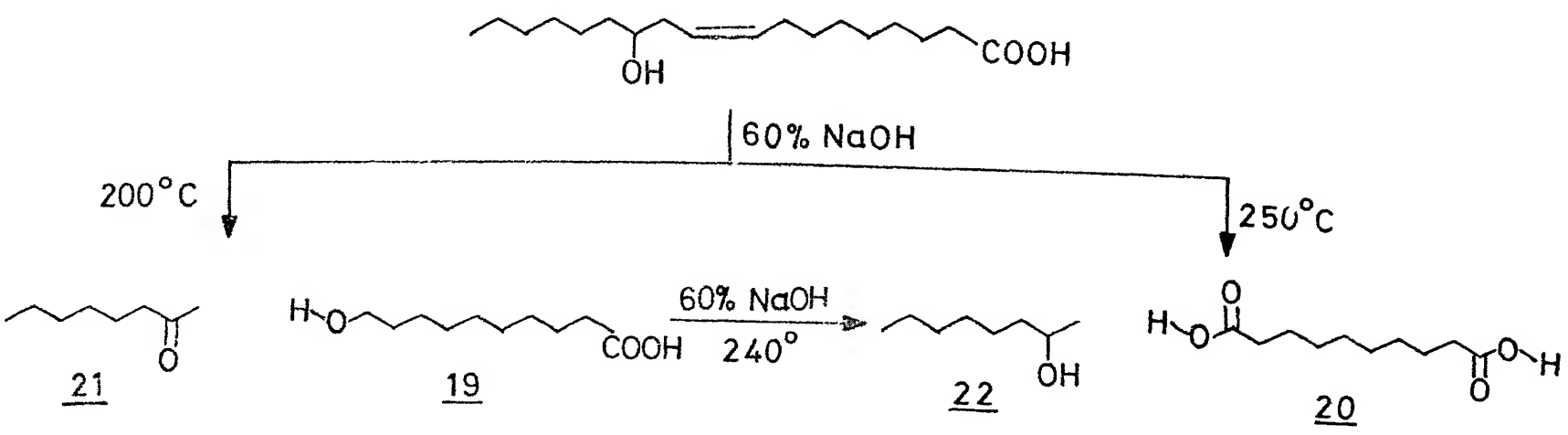
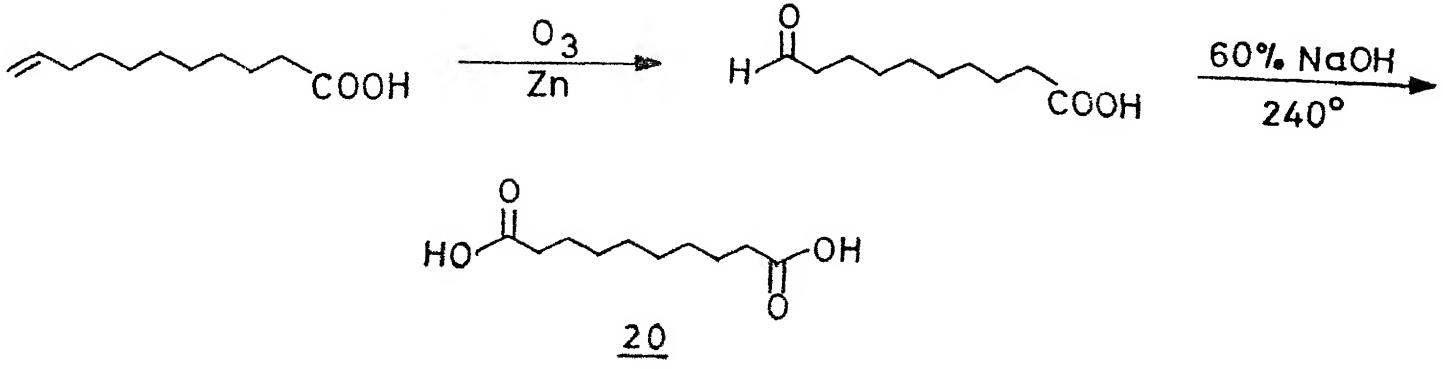


CHART II.C.10



hydride loss from the γ , δ -unsaturated alcohol (homoallyl alcohol) unit would spontaneously be transformed to the α , β - unsaturated ketone intermediate envisaged by Hargreaves and Owen .[24] Thus, the primary reaction, under all cleavage conditions, proceeds *via* sequence, γ,δ -unsaturated alcohol $\longrightarrow$ β , γ -unsaturated ketone $\longrightarrow$ α,β -unsaturated ketone $\longrightarrow$ β - hydroxy ketone $\longrightarrow$ ketone + aldehyde.

The events that take place further, are amenable to a variety of controls (*vide infra*). At 180°, the starting material ricinoleic acid,and the aldehyde component arising from the primary reaction , namely ,10-oxo decanoic acid, form an efficient redox pair leading to further cleavage by sequence outlined above. It is important to note that under these conditions 2-octanone is not able to influence the reaction and is, in effect, not involved either as an acceptor of hydride or as a redox partner. The situation changes dramatically at 240°. The aldehyde now is oxidised to sebacic acid, *via* uncoupled pathway, releasing hydride ions that could either reduce the carbonyl intermediates present in the milieu or pick up proton to form H_2, which is always observed. This facet has been experimentally demonstrated. Thus ,10-oxo-decanoic acid with 60% NaOH at 240° readily gives sebacic acid and hydrogen[29] (CHART II.C.10) : Coupled and uncoupled substrate oxidations co-exist at 240°. Since the primary process is required for

CHART II.C.11

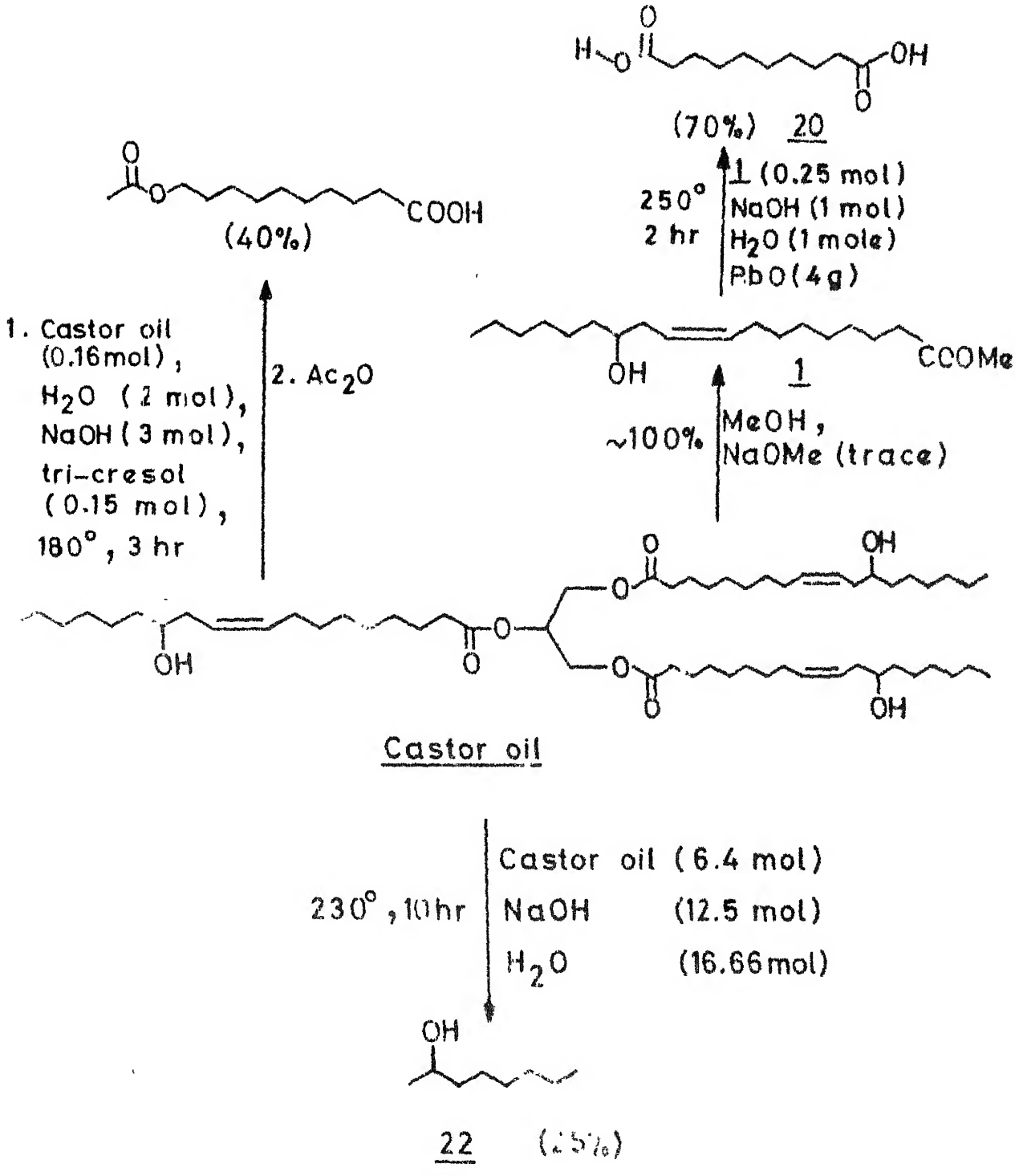
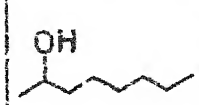

(70%) 20
250°
2 hr
1 (0.25 mol)
NaOH (1 mol)
H2O (1 mole)
PbO (4g)
(40%)
1. Castor oil (0.16mol), H2O (2 mol), NaOH (3 mol), tri-cresol (0.15 mol), 180°, 3 hr
2. Ac2O
1
~100%
MeOH, NaOMe (trace)
Castor oil
230°, 10hr
Castor oil (6.4 mol)
NaOH (12.5 mol)
H2O (16.66mol)
22 (25%)

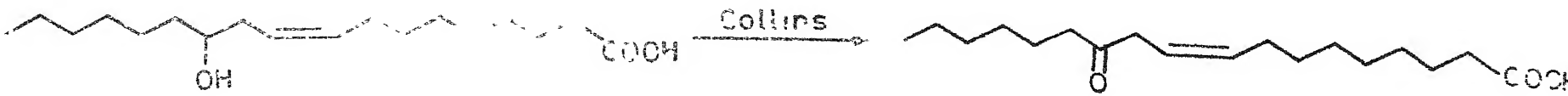
CHART II.C.12

Variants in the "base" thermolysis of castor oil

OH (mol)	NaOH (mol)	H_2O (mol)	Control (mol)	t °C	hr	$HO-(CH_2)_9-COOH$ (%)	$HOOC-(CH_2)_8-COOH$ (%)	Unreacted (%)
	[illegible]	[illegible]	nil	202	2.3	23	37	[illegible]
	2.75	0.5	 (0.38)	184	6.6	19	67	nil
	3.00	2	 (1.5)	183	11.5	80	11	nil

these phenomena, the 2-octanone immediately suffers reduction to 2-octanol ! Part of 2-octanol may arise from hydride reduction and the remaining via a ricinoleic acid ⟶ 2-octanone redox pair. Another pretty feature of this phenomenon is that the 10-oxo decanoic acid which plays such a pivotal role is a fragile substance and unless environment uses it up rapidly, it is transformed to intractable polymers ! This has been experimentally demonstrated.[30] The key α ,β -unsaturated ketone unit can be realised under mild conditions by treatment of 12-oxo(Z) 9-octadecenoic acid, available by Collins oxidation of ricinoleic acid, with dilute alkali. In the event, treatment of 12-oxo(Z) 9-octadecenoic acid with 0.03N NaOH at 100° gave 2-octanone (21) in 36% yield. The latter results from the anticipated sequence of events, namely, β ,γ -unsaturated ketone ⟶ α , β -unsaturated ketone ⟶ β -hydroxy ketone ⟶ ketone + aldehyde (CHART II.C.13). None of the expected 10-oxo-decanoic acid could be isolated since it underwent polymerisation.[29]

Since the 10-oxo decanoic acid ⟶ 1,10-decanedioic acid (20) change requires presence of excess alkali at 240°C, where the ricinoleic acid - 2 octanone redox system operate and since 10-oxo-decanoic acid efficiently forms a redox pair at 180° with ricinoleic acid, the importance of this key aldehyde in the reaction can be down-graded by letting it the option to polymerise. This can be neatly achieved with low alkali concentration at 240°C ! The objective of this would be to increase the



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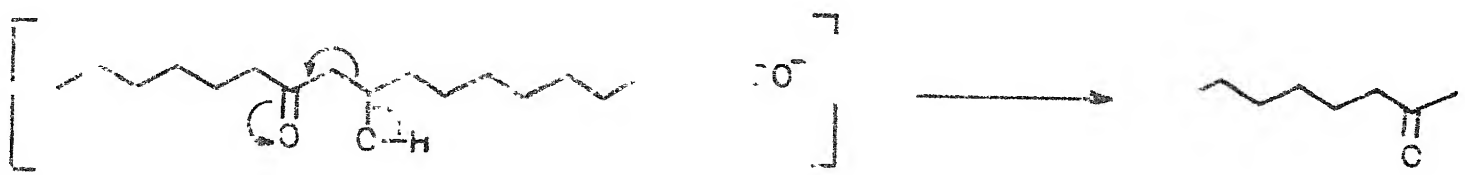


21 (35%)

yield of 2-octanol (vide infra). Thus, the alkali mediated castor oil cleavage could be achieved with focus in yield either on 10-hydroxy decanoic acid or 1,10-decanedioic acid (20) or 2-octanol (22). The practical realization of these is highlighted in CHART II.C.11.

The transformation of castor oil to sebacic acid (20) is an industrially important process, particularly with reference to the production of synthetic fibres. 2-Octanol is an industrial solvent and 10-hydroxy decanoic acid has been used in the synthesis of Queen bee pheromone.[31]

The controls illustrated in CHART II.C.11 pertain to only temperature of the reaction and amounts of alkali added. Diamond, Binder and Applewhite[32] demonstrated that the cleavage reaction can be made much more versatile by the introduction of external controls. They made a very careful study of castor oil fragmentation under alkaline conditions. The highlight of this work was that even at 180° the reaction can be channelized either towards 10-hydroxy decanoic acid or 1,10-decanedioic acid by introduction of proper controls (CHART II.C.12). Thus, external addition of 2-octanone dramatically tilted the reaction towards sebacic acid, even at 180°, via incorporation of an additional efficient 10-oxo decanoic acid $\longrightarrow$ 2 octanone redox system. On the other hand, addition of 2-octanol remarkably increased the yield of 10-hydroxy decanoic acid by operation of the

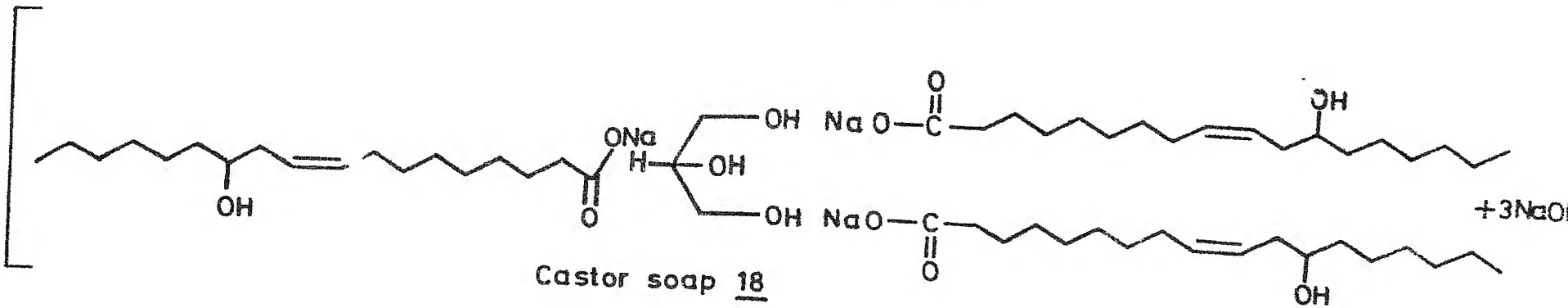
10-oxo decanoic acid - 2 octanol redox system (CHART II.C.12). It should therefore be possible not only to effect, the base involved castor oil cleavage, under mild conditions but also to direct the course of events to obtain desired products.

The genesis of the present work was the recipe provided by Adams and Marvel, in Organic Synthesis[33], for the preparation of 2-octanol in 23-25% yield by alkaline cleavage of castor oil. This procedure, different from all others, has several unusual features, the important one being, the prior formation of what is called the "castor soap" using a very low castor oil:sodium hydroxide ratio (CHART II.C.14).

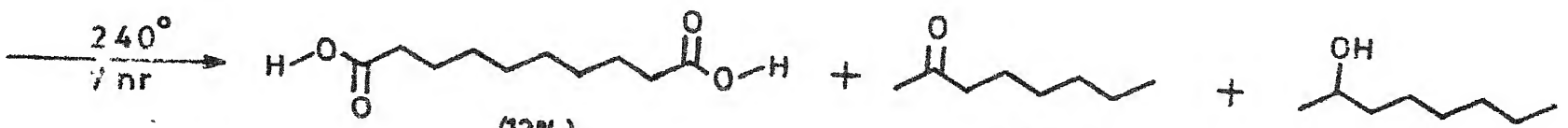
It was felt desirable to re-examine the pyrolysis of "castor soap" as well as to examine this readily available substance as a "hydride reagent". Although indirect evidence is in agreement with oxidation of substrates <u>via</u> hydride release, this facet has not been experimentally demonstrated in the alkaline thermolysis of castor oil itself.

"Castor soap" was readily prepared by addition of 2 moles of NaOH per mole of ricinoleic acid as an aqueous solution ($NaOH:H_2O::5:3$) to stirred castor oil. An ivory coloured hard soap is formed soon with evolution of considerable heat. It was found that such a soap is not formed when only one equivalent of NaOH was used. Two hundred and fifty gram lots of "castor soap" were prepared, pulverised thoroughly and used in all

CHART II.C.14



Castor soap 18



20 21 22

experiments. As expected of an acid-salt buffer, the pH of a molar solution was found to be 10. It is possible that the extra mole of hydroxide has been used up to a considerable extent *via* reaction with the hydroxyl functions present either in the ricinoleic acid or glycerol.

The "castor soap" melts around 220° and rapidly decomposes at 240°. One hundred grams of "castor soap" (18) was thermolysed at 220-240°, generally according to the procedure of Adams and Marvel,[33] for 7 hr and distilled. The distillate consisted of largely a mixture of 2-octanol (22) and 2-octanone (21) in a ratio of 2:1. The combined yield was a very remarkable 73%, vastly superior to that reported in Organic Synthesis. The boiling points of 2-octanol (22) and 2-octanone (21) being, respectively, 175° and 173°, they cannot be easily separated. From the practical viewpoint, the total distillate is best transformed either by PCC oxidation to 2-octanone (21) or by borohydride reduction to 2-octanol (22). Thus, "castor soap" is a very superior starting material for, either 2-octanone (21) or 2-octanol (22) (CHART II.C.14). Adams and Marvel made no attempts to isolate sebacic acid formed in the reaction. In the present work, the residue after distillation, on extraction with boiling water gave 12% yield of sebacic acid. The yield of the latter is poor and was so anticipated on the basis of experimental conditions (*vide supra*).

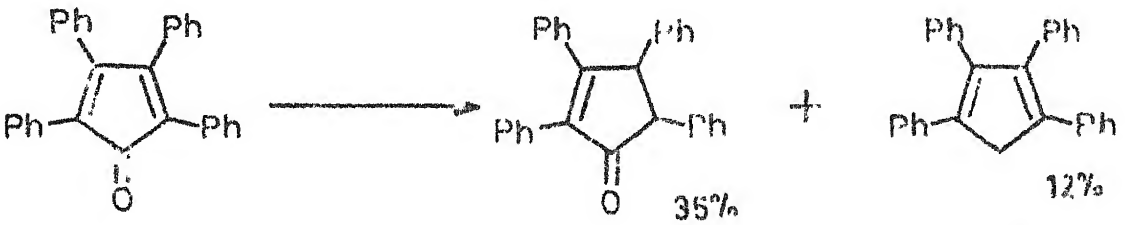
It turns out that "castor soap" is an efficient hydride equivalent and could bring about the reduction of a variety of substrates. The reduction of non-enolizable ketones has been illustrated with tetraphenylcyclopentadienone (tetracyclone 23), fluorenone, benzophenone and benzil. One mmole of these were mixed with 10g of"castor soap"(∿ 22 mmole hydride equivalent, taking into consideration only the primary step) and held at 240° for 2 hr. The results are presented in CHART II.C.15.

Tetracyclone gave not only 35% of the anticipated enone 24 but, surprisingly, also a 12% yield of tetraphenylcyclopentadiene (25). The latter is not easily made, the only satisfactory procedure being the reduction of tetracyclone with LAH + $AlCl_3$.[34] Blank experiments showed that the enone 24 is not an intermediate in the formation of the hydrocarbon 25. The transformation of 23 to 24 + 25 is rationalised in CHART II.C.16. The hydride acceptance leads to tetraphenylcyclopentadienol, which is known to be rapidly converted to enone 24 via prototropic shift. Therefore, the hydrogenolysis of the dienol to the hydrocarbon 25 should effectively compete with the prototropic shift. It should be possible to enhance the yield of the desirable hydrocarbon, 25 by choice of reaction conditions.

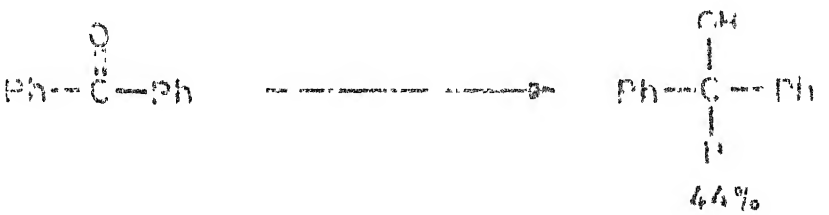
Fluorenone gave a 34% yield of fluorene. The intermediate fluorenol was not present. On the other hand, in the case of benzophenone, the reduction stopped at the first hydride

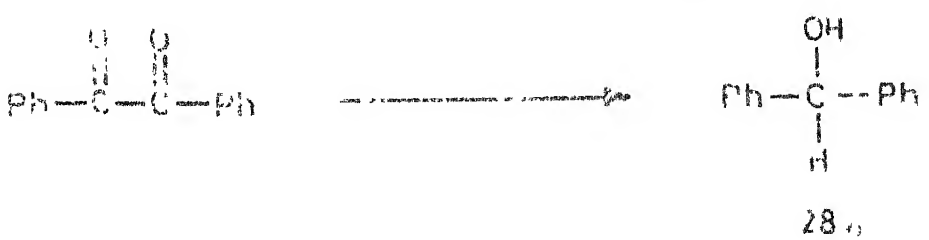
CHART II.C.15

Reduction of non-enolizable ketones with castor soap (18) at 240°C for 2 hr

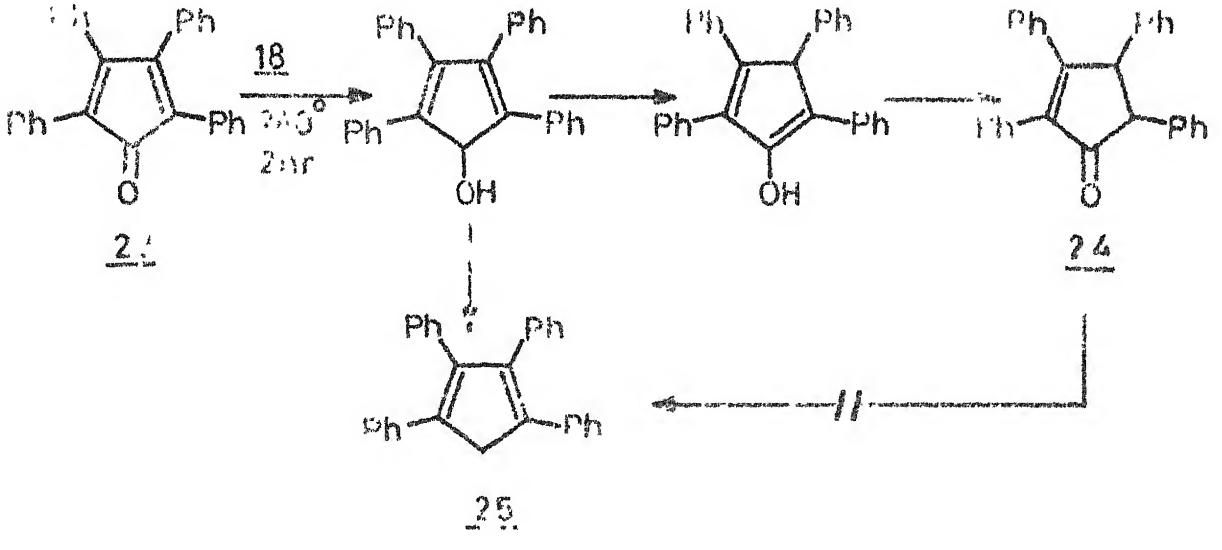


23 24 25





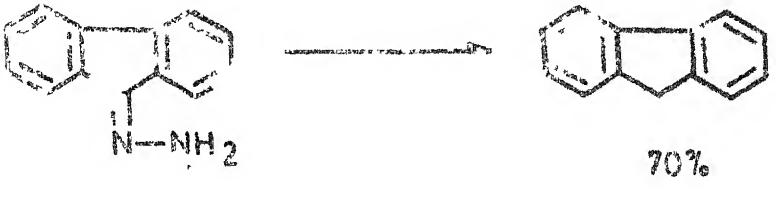
CHAPITRE II.C.16

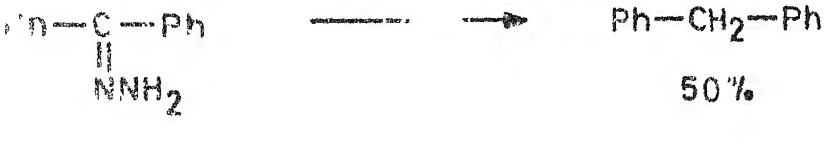


CHAPITRE II.C.17

"Wolff-Kishner" reduction with "water soup"

at 240° for 4 hr.





acceptance stage, leading to a 44% yield of benzydrol. Benzil, surprisingly, gave a 28% yield of benzydrol, whose formation, however, could be readily rationalized on the basis of a benzilic acid type rearrangement, fragmentation to benzophenone + carbon monoxide and reduction.

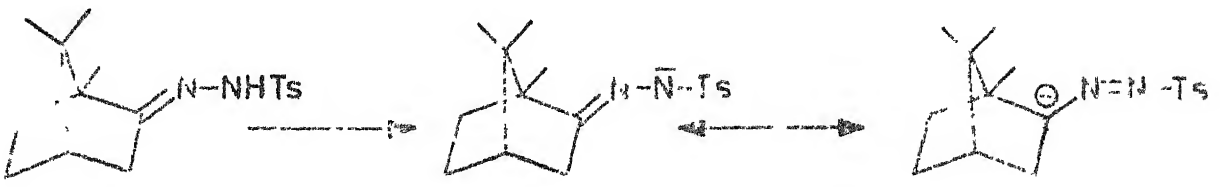
The "castor soap" is an even more effective medium for Wolff-Kischner reductions. Thus 20 mmol quantities of either fluorenone hydrazone or benzophenone hydrazone when admixed with 20g "castor soap" (∿ 42 mmol hydride equivalent) and thermolysed for 4 hr at 240°, gave fluorene (70%) and diphenylmethane (50%).

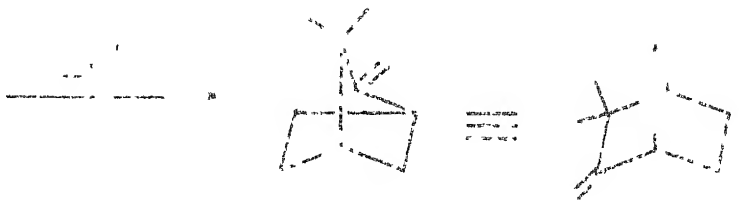
A remarkable transformation brought about with "castor soap" is the camphor tosylhydrazone (26) ⟶ camphene (27) change, accomplished in 80% yields by thermolysis of 20 mmoles of 26 with 10g of "castor soap" (∿ 22 mmol hydride equivalent) at 240° for 3 hr and which can be rationalized on the basis of formation and decomposition of carbenic intermediates in a proton available media (CHART II.C.18). The overall transformation proceeds via sequence, conjugate base formation with hydride, extrusion of N_2 and Ts^- leading to a carbenic intermediate, proton acceptance by the latter to form camphane 2 cation, σ shift and proton loss.

"Castor soap" has been found to be an efficient agent for the reduction of aromatic nitro compounds to amines. Thus

CHART II.C.18

The generation of carbenic intermediate with "castor-soap" at 240° for 3 hr.





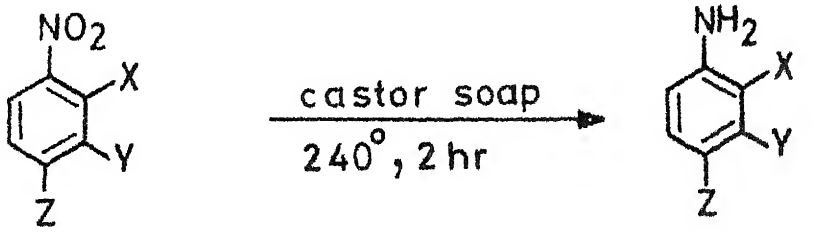
21

excellent yields are obtained upon thermolysis of 20 mmoles of nitro compounds with 30g (60 mmol hydride equivalent) of"castor soap"at 240^{o} for 2 hr (CHART II.C.19).

The present work has hopefully brought to focus the multifacetted nature of the, apparently trivial, cleavage of castor oil under alkaline conditions. The salient features pertaining to possible events that are likely to occur are presented in CHART II.C.20. It appears that the benefits arising from the understanding of this transformation with all possible manifestations, as illustrated in CHART II.C.20, should be considerable. Thus, the course of events could be further controlled to optimize yields, the cleavage could be achieved under milder conditions, the redox partners could be changed, the theme of co-existence of several redox systems could be transplanted in other substrates and efficient and inexpensive reagents could be developed based on such an understanding.

CHART II.C.19

Reduction of aromatic nitro compounds with "castor soap".



X	Y	Z	Yield (%)*
H	H	H	56***
CH_3	H	H	81
H	CH_3	H	95
H	H	CH_3	84
NH_2	H	H	93
H	H	Cl	88
NO_2	H	H	91**

* Isolated as picrates

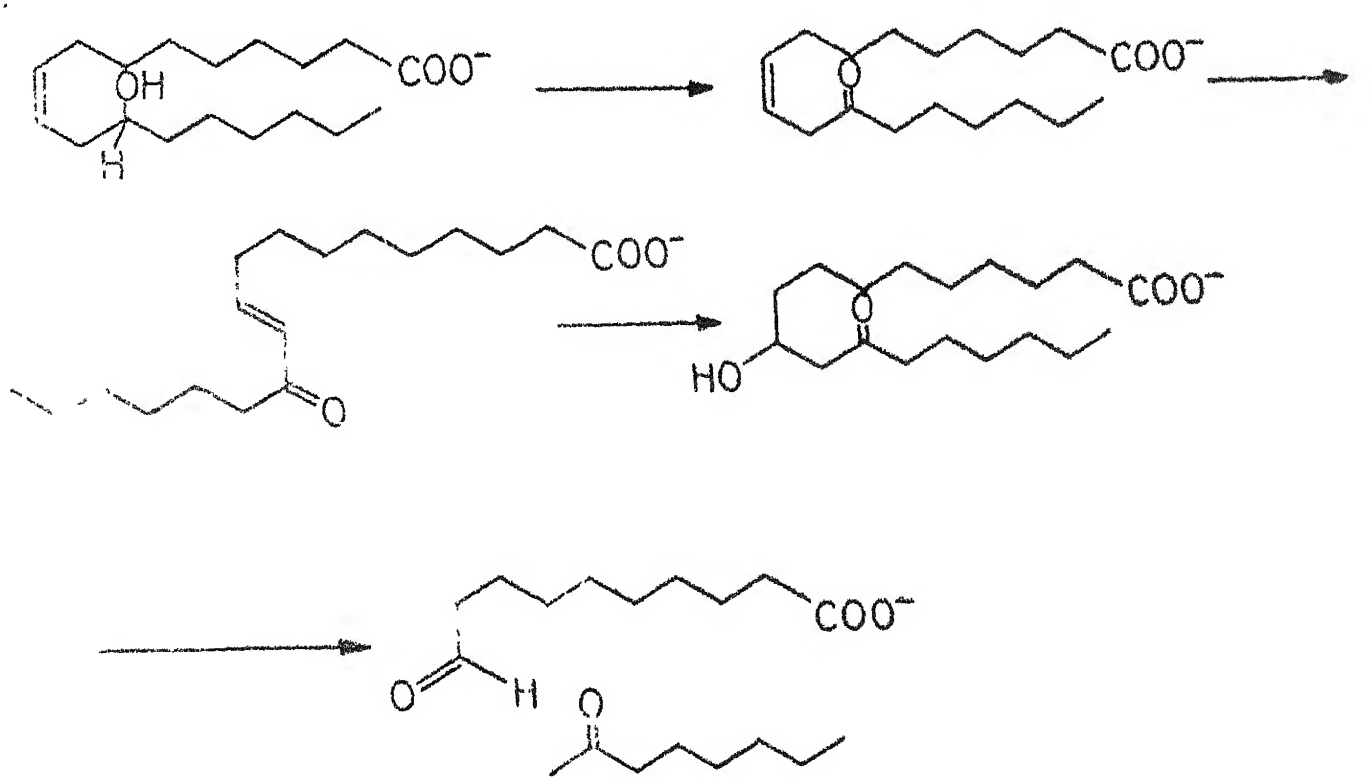
** O-phenylene diamine

*** Isolated aniline

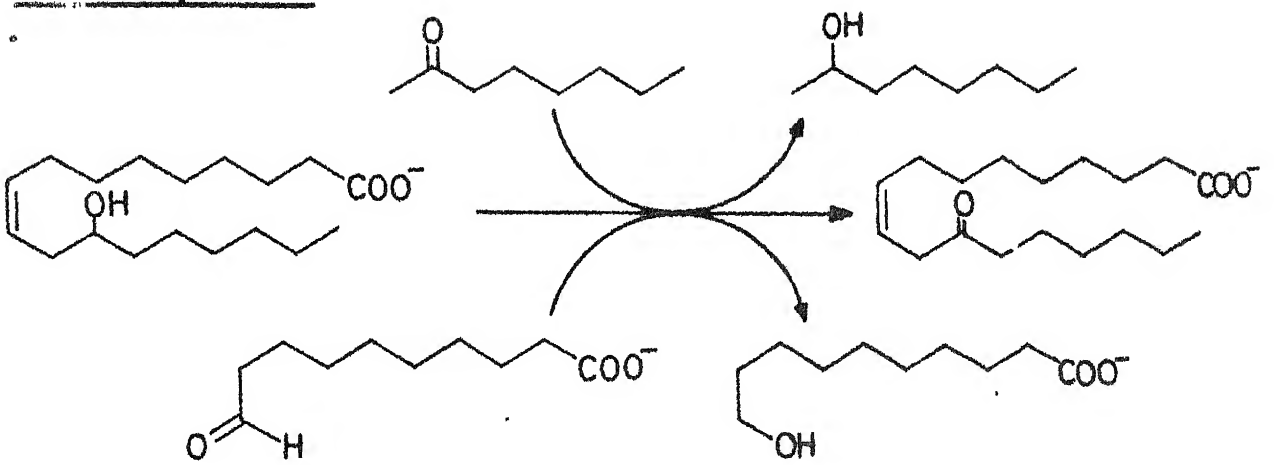
CHART II.C.20

A comprehensive description of the thermolysis of castor oil under alkaline condition.

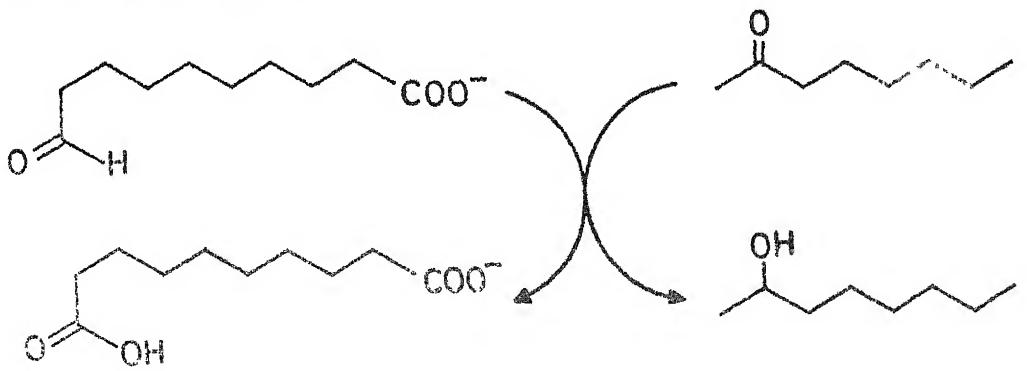
Primary reaction



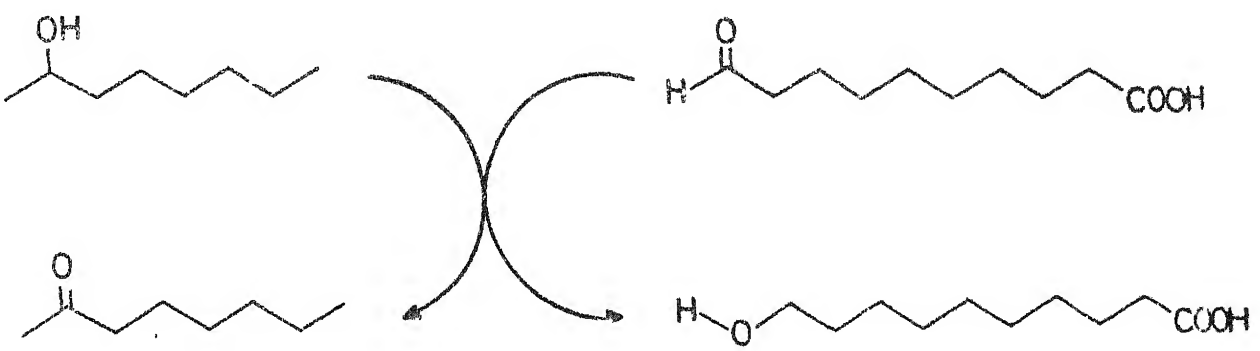
Redox system I



Redox system II



Redox system III



II.D. EXPERIMENTAL

Melting points and boiling points are uncorrected. Infrared spectra were recorded on Perkin-Elmer, Model-580 spectrophotometer as thin films for liquids and KBr discs for solids. NMR spectra were obtained on approximately 10-15% solutions in $CDCl_3$ and CCl_4 on TR-90 spectrometer. The chemical shifts are reported in parts per million downfield from tetramethylsilane at 0.00 as internal standard. Silica gel G(Acme) was used for thin layer chromatography and column chromatography was done on silica gel (Acme, 100-200 mesh), columns were prepared from its slurry in petroleum ether (60-80°). Reactions were monitored, wherever possible, by tlc.

I. The transformation of castor oil to methyl 12-hydroxy octadecynoate(3)

a. 12-Hydroxy 9-octadecynoic acid (2)

Bromine (40g, 0.25 mol) was added in a thin stream to a well stirred and cooled (-30°) solution of castor oil (70g, 0.075 mol) in ethyl alcohol (40 ml). The reaction mixture was allowed to reach RT, admixed with a solution of KOH (80g, 1.43 mol) in water (50 ml), refluxed for 10 hr, poured on to ice-water (500 ml), acidified with cold H_2SO_4 (5N), left aside overnight,

extracted with ether, dried and solvents evaporated to give 55.7g (85%) of 2 which crystallised from petroleum ether; mp 47° (lit.[35] mp 49-50°).

ir: ν_{max}(neat)(cm^{-1}): 3468 (hydroxyl), 1710 (acid).

b. Fischer-esterification of 12-hydroxy 9-octadecynoic acid: Preparation of methyl 12-hydroxy 9-octadecynoate (3)

A mixture of 2 (30g, 0.01 mol), dry methanol (500 ml), and H_2SO_4 (0.5 ml) was refluxed for 4 hr, solvents evaporated, the residue poured on to ice-water (300 ml), extracted with ether (3x150 ml), washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to give 30g (95%) of 3, bp 130-135°/0.05 torr.

ir: ν_{max}(neat)(cm^{-1}): 3420 (hydroxyl), 1740 (ester).

II. Thermal fragmentation of methyl 12-hydroxy octadecynoate(3) to methyl 9,10-undecadienoate(4) and heptanal

Under a set-up for distillation 3 (25g, 0.08 mol), evenly supported on clean sand (∿ 5g) was heated for 0.5 hr with a Bunsen burner over a luminous flame. The distillate (22g) on fractionation gave 5g (71%) 4, bp 75-78°/0.07 torr and unchanged 3 (14g), bp 130-135°/0.05 torr.

Anal. Calcd. for $C_{12}H_{20}O_2$ (Mol. Wt. 196)

C, 73.47; H, 10.2%

Found C, 73.69; H, 9.87%

ir : ν_{max}(neat)(cm^{-1}): 1950 (allene), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 2.15 (m, 4H, $-C\underline{H}_2COOCH_3$, $=CH-C\underline{H}_2-CH_2$)
3.5 (s, 3H, $-COOC\underline{H}_3$), 4.45 (qq,2H, $C\underline{H}_2=C=C-H$),
4.9 (m, 1H, $CH_2=C=C\underline{H}-CH_2$).

III. Reaction of methyl 10-undecenoate with chloral. Attempted preparation of methyl 12-trichloromethyl 12-hydroxy(E) 9-dodecenoate (6)

Under a set-up for removal of water a solution of chloral hydrate (1.98g, 0.012 mol) in benzene (50 ml) was refluxed for 4 hr, admixed with methyl 10-undecenoate (1.98g, 0.01 mol) and reflux continued for an additional 4 hr. TLC showed essentially no change. Another lot of chloral hydrate (6g; 0.036 mol) was introduced and the mixture refluxed for 8 hr. The reaction mixture was poured on to ice-water, extracted with ether, dried ($MgSO_4$) and solvents evaporated. Elemental analyses of the residue showed no chloral incorporation and IR revealed extensive transformation of the ester to the acid.

IV. Collins oxidation of methyl ricinoleate (1): Preparation of methyl 12-oxo oleate (7)

A solution of methyl ricinoleate (1) (6.24g, 0.02 mol), in dry dichloromethane (20 ml), was added, dropwise at RT, to stirred Collins reagent [prepared from chromium trioxide (12g, 0.12 mol) and pyridine: dichloromethane::1:10, 220 ml], left

stirred for 24 hr, decanted, the residue washed with dry dichloromethane (20 ml), the combined extracts washed with aqueous sodium sulphite (5%), hydrochloric acid (5%), chilled water, dried ($MgSO_4$) and solvents evaporated to give 6g of 7 which was chromatographed on silica gel. Elution with benzene:ethyl acetate::85:15 gave 4.8g (84%) of 7; bp 125°/0.05 torr.

ir : ν_{max}(neat)(cm^{-1}): 1740 (ester), 1715 (carbonyl).

nmr: $\delta_{(CDCl_3)}$: 5.55 (t, J=5Hz, olefin), 3.65 ($COOCH_3$), 3.15 (d, J=5 Hz, $=CH-CH_2-C=O$).

V. Addition of PhMgBr to methyl 12-oxo oleate: Preparation of diol 8

To a well stirred solution of PhMgBr [prepared from 1.0g Mg (0.04g atom) and 6.28g (0.04 mol) of bromobenzene] in ether (250 ml) was added, in drops, over 0.5 hr, keeping the temperature below 20°, a solution of 7 (2.96g, 0.01 mol) in ether (50 ml). The mixture was left stirred for 15 hr, the Grignard complex decomposed with 2N H_2SO_4, extracted with ether, washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and solvents evaporated to give 3.5g (78%) of 8 which was used as such in the following experiment.

ir: ν_{max}(neat)(cm^{-1}): 3420 (hydroxyl), 1600 (phenyl).

VI. Thermolysis of diol 8: Attempted preparation of hexyl phenyl ketone 9 and diene

Under a set-up for distillation, the diol 8 (2.5 g, 0.005 mol) supported evenly on clean sand (5 g) was thermolysed using a luminous flame for 1 hr at 400°C. The reaction mixture was cooled, extracted with benzene, solvents evaporated and the residue chromatographed. Elution with hexane:benzene::20:80 gave 1.8 g (78%) of 10.

ir : ν_{max} (neat) (cm^{-1}): 1650, 970 (double bond), 1600 (phenyl).

VII. Thermolysis of phenyl, (E) 2-butenyl methanol (11) to 1-butene and benzaldehyde.

a. Preparation of phenyl, (E) 2-butenyl methanol (11)

To a well stirred solution of crotyl magnesium bromide [prepared from 4.32g (0.18g atom) Mg and 18.5g (0.15 mol) crotyl bromide] in ether (200 ml) was added, in drops, over 0.5 hr, keeping the temperature below 25°, a solution of benzaldehyde (11.72g, 0.11 mol) in ether (50 ml). The reaction mixture was left stirred for 2 hr, the Grignard complex decomposed with

satd. NH_4Cl, extracted with ether, washed with brine, dried ($MgSO_4$), solvents evaporated and the residue on distillation gave 17.5g (60%) of 11, bp 55-58°/0.05 torr.

Anal. Calcd. for $C_{11}H_{14}O$ (Mol. Wt. 162)
C, 81.48; H, 8.64%
Found C, 81.73; H, 8.23%

ir : ν_{max}(neat)(cm^{-1}): 3450 (hydroxyl), 1640 (double bond), 1600 (phenyl).

nmr: $\delta_{(CCl_4)}$: 2.1-2.6 (m, 5H, CH_3-CH=CH_2-, allyl -CH_2), 4.3 (t, t proton), 5.0 (m, 2H, $H_2C{=}C\lessdot^{H}$), 5.6 (m, 1H, $H_2C{=}C\lessdot^{H}$).

b. Thermolysis of 11: Isolation of benzaldehyde

The alcohol 11 (1.541g, 0.009 mol) was evenly supported on glass wool, stabilized with a little hydroquinone and thermolysed for 1 hr at 400° using a flame. The reaction mixture was cooled, extracted with benzene, solvents evaporated and the residue treated with excess semicarbazide hydrochloride to give 1g (73%) of benzaldehyde semicarbazone, mp 223°C whose properties (mp, tlc, ir) were in good agreement with an authentic sample.

VIII. A novel procedure for the preparation of PhCOD

a. Oxidation of phenyl, (E) 2-butenyl methanol (11): Preparation of phenyl, (E) 2-butenyl ketone (12)

To a well stirred suspension of PCC (6.45g, 0.03 mol) in dry dichloromethane (10 ml), at RT, was added, in drops, a solution of 11 (3.23g, 0.02 mol) in dry dichloromethane (5 ml). The reaction mixture was left stirred for 2 hr at RT, admixed with ether (150 ml), passed through a small column of $MgSO_4$ and evaporated to give 2.746g (85.6%) of 12.

ir: ν_{max}(neat) (cm^{-1}): 1700 (carbonyl), 1650 (double bond), 1600 (phenyl).

b. Sodium borodeuteride reduction of phenyl, (E) 2-butenyl ketone (12): Preparation of phenyl, deutero, (E) 2-butenyl methanol (13)

To a well stirred suspension of $NaBD_4$ (0.213g, 0.007 mol) in dry THF (20 ml), at RT, was added a solution of 12 (1.335g, 0.008 mol) in dry THF (10 ml). The reaction mixture was refluxed for 1 hr, excess reagent decomposed by addition of water, extracted with ether, washed with brine, dried ($MgSO_4$), solvents evaporated and the residue on distillation gave 1.215g (93%) of 13; bp 110-115°/3 torr.

ir: ν_{max}(neat) (cm^{-1}): 3400 (hydroxyl), 2140 (C-D), 1640 (double bond), 1600 (phenyl).

c. Thermolysis of phenyl, deutero, (E) 2-butenyl methanol (13): Preparation of PhCOD

The deuterated alcohol 13 (1.2g, 7.5 mmol) on thermolysis as described in Experiment VII.b for the related 11 ⟶ benzaldehyde change gave 0.429g (93.4%) deuterobenzaldehyde semicarbazone, mp 218-221°, and unchanged 13 (0.76g), bp 110-112°/3 torr.

ir : ν_{max}(neat)(cm^{-1}): 3460 (N-H), 2210 (C-D), 1690(-$CONH_2$).

MS : m/e: 164 $(M)^+$

IX. Thermolysis of phenyl, 3 propenyl methanol (14) to benzaldehyde and propene

a. Phenyl 3-propenyl methanol (14)

To a well stirred solution of allyl magnesium bromide [prepared from 2.16g (0.09 g atom) Mg and 9.168g (0.075 mol) allyl bromide] in ether (150 ml) was added, in drops, over 0.5 hr, keeping the temperature below 25°, a solution of benzaldehyde (5.3g, 0.05 mol) in ether (50 ml). The reaction mixture was left stirred for 2 hr and work-up as described in Experiment VII.a for the preparation of the related 11 gave 8.1g (71.5%) of 14, bp 65-67°/0.1 torr.

Anal. Calcd. for $C_{10}H_{12}O$ (Mol. Wt. 148)
C, 81.35; H, 8.1%
Found C, 80.97; H, 8.34%

ir : ν_{max}(neat)(cm^{-1}): 3400 (hydroxyl), 1640 (double bond), 1600 (phenyl).

nmr: $\delta_{(CDCl_3)}$: 2.2 (br t, allyl -C<u>H</u>$_2$), 3.1 (br, -O<u>H</u>), 4.4 (t, t proton), 5.0 (br d, <u>H</u>$_2$C=C$\overset{\underline{H}}{<}$), 6.5 (m, H$_2$C=C$\overset{\underline{H}}{<}$).

b. Thermolysis of phenyl, 3-propenyl methanol (<u>14</u>)

Thermolysis of <u>14</u> (1.519g, 0.01 mol) as described in Experiment VII.b for the related <u>12</u> ⟶ benzaldehyde change gave 0.662g (39%) of benzaldehyde semicarbazone, mp 224°.

X. Thermolysis of p-toluyl, 3-propenyl methanol (<u>15</u>) to p-tolualdehyde and propene

a. Preparation of p-toluyl, 3-propenyl methanol (<u>15</u>)

The reaction of allyl magnesium bromide [prepared from 2.216g (0.09 g atom) Mg and 9.0g (0.075 mol) allyl bromide] with p-tolualdehyde (6.0g, 0.05 mol) as described in Experiment VII.a and IX.a gave 7.9g (65.8%) of <u>15</u>, bp 80-82°/0.15 torr.

Anal. Calcd. for $C_{11}H_{14}O$ (Mol. Wt. 162)
C, 81.48; H, 8.64%
Found C, 81.51; H, 8.79%

ir : ν_{max}(neat)(cm^{-1}): 3400 (hydroxyl), 1635 (double bond), 1610 (phenyl).

nmr: $\delta_{(CDCl_3)}$: 2.2 (m, 5H, ar $-C\underline{H}_3$, allyl $-C\underline{H}_2$), 3.1 (s,1H, $-O\underline{H}$), 4.3 (t, 1H, t proton), 4.9 (br d, 2H, $H_2C{=}C\!<^{H}$), 5.6 (m, 1H, $H_2C{=}C\!<^{\underline{H}}$).

b. Thermolysis of p-toluyl 3-propenyl methanol (15)

Thermolysis of 15 (1.586g, 0.0095 mol) as described in Experiment IX.b for the related 14 ⟶ benzaldehyde change, gave 1.2g (70.6%) of p-tolualdehyde semicarbazone, mp 230-232°.

XI. Thermolysis of p-nitrophenyl, 3-propenyl methanol (16) to p-nitrobenzaldehyde and propene

a. Preparation of p-nitrophenyl, 3-propenyl methanol (16)

The reaction of allyl magnesium bromide [prepared from 0.502g (0.02 g atom) Mg and 1.9g (0.015 mol) allyl bromide] and p-nitrobenzaldehyde (1.5g, 0.01 mol), as described in Experiment VII.a and IX.a followed by chromatography of the crude product over silica gel and elution with benzene:ethyl acetate::80:20 gave 1.32g (67%) of 16, bp 55-60°/0.2 torr.

ir : ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl), 1530, 1340 (nitro).

b. Thermolysis of p-nitrophenyl, 3-propenyl methanol (16)

Thermolysis of 16 (1.5 g, 0.008 mol) as described in Experiment IX.b for the related 14 ⟶ benzaldehyde change, gave 0.209 g (18%) of p-nitrobenzaldehyde, mp 104°.

XII. Thermolysis of 3-hydroxy, 3-phenyl 1-pentene (17) to acetophenone and propene

a. Preparation of 3-hydroxy, 3-phenyl 1-pentene (17)

The reaction of allyl magnesium bromide [prepared from 2.21 g (0.009 g atom) Mg and 9.128 g (0.075 mol) allyl bromide] with acetophenone (6g, 0.05 mol), as described in Experiment VII.a and IX.a gave 8.7 g (72.5%) of 17, bp 62-64°/0.07 torr.

Anal. Calcd. for $C_{11}H_{14}O$ (Mol. Wt. 162)
C, 81.48; H, 8.64%
Found C, 81.71; H, 8.49%

ir : ν_{max}(neat)(cm^{-1}): 3440 (hydroxyl), 1640 (double bond), 1600 (Phenyl).

nmr: $\delta_{(CCl_4)}$: 1.5 (s, 3H, $-C\underline{H}_3$), 2.2 (s, 1H, $-O\underline{H}$), 2.5 (t, 2H, allyl $-C\underline{H}_2$), 5.0 (br d, 2H, $H_2C{=}C\langle^{H}$), 5.6 (br, $H_2C{=}C\underline{H}{-}CH_2{-}$).

b. Thermolysis of 3-phenyl, 3-hydroxy 1-pentene (17)

Thermolysis of 17 (1.428g, 0.009 mol) as described in Experiment IX.b for the related 14 ⟶ benzaldehyde change gave 0.841g (57%) of acetophenone semicarbazone, mp 196°.

XIII. Preparation of "castor soap" (18)

To hand-stirred castor oil (190g, 0.2 mol) in a china dish was added gradually a solution of NaOH (50g, 1.25 mol) in water (30 ml). The reaction mixture sets into a hard mass with considerable evolution of heat. The ivory colored castor soap thus formed was pulverised thoroughly. An aqueous molar solution showed a pH of 10, thus demonstrating a buffer system.

XIV. Thermolysis of "castor soap". Formation of 1,10-decanedioic acid (20), 2-octanone (21) and 2-octanol (22)

Neat "castor soap" (18) (100g, ∿ 0.074 mol) was heated with a Bunsen burner. The castor soap melts and gradually decomposes. The inside temperature never rises above 240°C. The course of the reaction can be monitored by the presence of misty vapours above the reaction mixture as long as decomposition is in progress, which usually lasts for 7 hr. The volatile products were removed by slow distillation, lasting 4 hr. The distillate on fractionation gave 18.9g of fraction consisting essentially of 2-octanol (22) and 2-octanone (21) in the ratio 2:1.

This analysis was done on the basis of isolation of crystalline 2-octanone semicarbazone, mp 121°. The estimated yields of 2-octanol and 2-octanone are respectively, 49% and 24%. The residue was repeatedly extracted with boiling water and cooled to give 5.0g (12%) of sebacic acid (20), mp 131° (lit. mp 133°).

XV. Reduction of non-enolizable ketones with "castor soap"

a. General procedure

An intimate mixture of the ketone (10 mmol) and "castor soap" (18) (10g; ∿ 22 mmol hydride equivalent) was held at an inside temperature of 240°, by a Bunsen flame, for 2 hr, cooled digested with water, extracted with ether, washed with brine, dried ($MgSO_4$), solvents evaporated and the residue chromatographed on silica gel. The products were isolated by elution with solvents appropriate in each case.

b. Reduction of tetraphenylcyclopentadienone (23): Isolation of enone 24 and tetraphenylcyclopentadiene (25)

Elution with benzene:hexane::40:60 gave 0.453g (12.3%) of 25, mp 184°.

Anal. Calcd. for C_9H_{22} (Mol. Wt. 370)
C, 94.04; H, 5.94%
Found C, 94.04; H, 5.63%

Further elution with benzene gave 1.346g (35%) of 24, mp 156°, whose ir and mp were identical to that of an authentic sample. Blank experiment showed that 24 is not transformed to 25 on further treatment with "castor soap" at 240°C.

c. Reduction of fluorenone: Isolation of fluorene

Elution with benzene:hexane::25:75 gave 0.504g (34%) of fluorene, mp 110-113°, whose ir was identical to that of an authentic sample.

d. Reduction of benzophenone: Isolation of benzhydrol

Elution with benzene:ethyl acetate::85:15 gave 0.797g (43%) of benzhydrol, mp 64-66°, whose ir was identical to that of an authentic sample.

e. Reaction of benzil with "castor soap": Isolation of benzhydrol

Elution with benzene:ethyl acetate::80:20 gave 0.504g (28%) of benzhydrol, mp 63-64°, identical to that of an authentic sample.

XVI. "Wolff-Kischner" reduction with "castor soap"

a. General procedure

An intimate mixture of the hydrazone (∿ 20 mmol) and castor soap (20g, ∿ 44 mmol hydride equivalent) was held at 240°

for 4 hr, using a flame, cooled, digested with water, extracted with ether, washed with brine, dried ($MgSO_4$), solvent evaporated and the residue chromatographed on silica gel. Elution with hexane:benzene::90:10 gave the hydrocarbon.

b. Reduction of fluorenone hydrazone to fluorene

Elution with benzene:hexane::1:9 gave 1.735g (70%) of fluorene, mp 112-114°, from 15 mmol of fluorenone hydrazone.

c. Reduction of benzophenone hydrazone to diphenylmethane

Elution with benzene:hexane::1:9 gave 1.75g (50%) of diphenylmethane, mp 26°, from 20 mmol of benzophenone hydrazone.

XVII. Demonstration of the generation of carbenic intermediates in the "castor soap" mediated decomposition of camphor tosyl hydrazone (26): Isolation of camphene (27)

An intimate mixture of camphor tosylhydrazone (26) (3.2g, 0.02 mol) and "castor soap" (20g, ∿ 44 mmol hydride equivalent) was held at 240°, using a flame, cooled, digested with water, extracted with ether, washed with brine, dried ($MgSO_4$), solvents evaporated and the residue on chromatography over silica gel and elution with hexane:benzene::80:20 gave 1.2g (80%) of camphene (27) whose ir and nmr was identical to that of an authentic sample.

nmr: $\delta_{(CCl_4)}$: 4.55(s), 4.75(s), ($=CH_2$), 2.7 (br s, allylic t proton).

XVIII. Transformation of aromatic nitro compounds to amines by reduction with "castor soap" (18)

An intimate mixture of the aromatic nitro compound (20 mmol) and "castor soap" (30g; 66 mmol of hydride equivalent) was held at 240° for 2 hr, using a flame, the reaction mixture was then distilled and an aliquot converted to the picrate derivative.

Thus, o-toluidine (81%), m-toluidine (95%), p-toluidine (84%) and p-chloroaniline (88%) were obtained from the corresponding nitro precursors. O-dinitrobenzene as well as o-nitroaniline gave o-phenylene diamine in respectively, 91% and 93% yields. In case of aniline no picrate formed and it was isolated as such in 56% yield.

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VITAE

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